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Modified A-DROP score and mortality in hemodialysis patients with pneumonia

Makoto Harada^{1,2*}, Takeshi Masubuchi^{3,4}, Kazuaki Fujii^{1,2}, Yukifumi Kurasawa^{1,2}, Tohru Ichikawa¹ and Mamoru Kobayashi¹

Abstract

Background: Pneumonia is common in hemodialysis (HD) patients and has a poor prognosis, but there is little information on an accurate method for evaluating the severity of pneumonia, which is closely associated with prognosis, in HD patients. This study examined a method for evaluating the severity of pneumonia that was closely associated with 30-day mortality in HD patients.

Methods: This was a retrospective observational study of 64 HD patients. We determined the relationship between the severity of pneumonia using a modified A-DROP (excluding the dehydration section) score and 30-day mortality.

Results: Nine patients (14.1%) died and 40% of patients with an A-DROP score of 3 or 4 died within 30 days. Logistic regression analysis showed that the A-DROP score was significantly associated with 30-day mortality. The discriminatory ability of the A-DROP score was assessed using area under the receiver operating characteristic curve analysis (0.810; 95% confidence interval 0.653–0.967; p < 0.01).

Conclusions: This modified A-DROP scoring system reflected the severity of pneumonia and was significantly associated with 30-day mortality. Patients with a modified A-DROP score of 3 or 4 had a poor prognosis.

Keywords: Pneumonia, Hemodialysis patients, A-DROP score

Background

Infectious diseases are one of the main causes of death among hemodialysis (HD) patients, and respiratory infectious diseases, especially pneumonia, are common and resulting in high mortality [1, 2]. HD patients who develop pneumonia are often difficult to treat because they are immune-compromised. They also tend to be elderly, and controlling the antibiotic dose is important [1, 2]. HD patients are also at high risk for blood stream-related infections [3] and methicillin-resistant *Staphylococcus aureus* or drug-resistant bacterial infections [4].

Pneumonia that develops in HD patients is included under the definitions of healthcare-associated pneumonia (HCAP) [5] and nursing and healthcare-associated pneumonia (NHCAP) [6]. Previous reports have suggested that the bacteria causing pneumonia are the same

* Correspondence: tokomadaraha@yahoo.co.jp

in HD and HCAP patients [4, 7]. However, when evaluating the severity of pneumonia, it is important to differentiate pneumonia in HD patients from HCAP.

There are several scoring systems used to evaluate the severity of community-acquired pneumonia, such as the pneumonia severity index (PSI), CURB65, and A-DROP [8–10]. PSI is a well-known but complex index that includes blood urea nitrogen and pleural effusion and is strongly influenced by dialysis. CURB65 and A-DROP also include blood urea nitrogen [8–10].

It is possible that pneumonia in patients with HD should be distinguished from non-HD patients with HCAP. The method for evaluating the severity of pneumonia in HD patients has not been fully investigated, and the relationship between the severity of pneumonia and prognosis in HD patients is not completely understood.

The Japanese Respiratory Society has recommended that the A-DROP score is used for evaluating the severity of community-acquired pneumonia (CAP) [10]. The A-DROP score is well-known and widely used in Japan. Although the A-DROP score is used for CAP and



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¹Department of Nephrology, Nagano Red Cross Hospital, 5-22-1, Wakasato, Nagano 380-8582, Japan

²Department of Nephrology, Shinshu University School of Medicine, 3-1-1, Asahi, Matsumoto 390-8621, Japan

Full list of author information is available at the end of the article

pneumonia in HD patients categorized as NHCAP [6], a previous report suggests that a very high A-DROP score should be included as a prognostic factor for NHCAP [11]. In the current study, we adopted an A-DROP score based on a new scoring method, a "modified A-DROP score," to evaluate the severity of pneumonia. The modified A-DROP score did not include the dehydration section. We aimed to clarify the usefulness of the modified A-DROP score for evaluating the severity of pneumonia, which is significantly associated with prognosis in HD patients.

Methods

Study design

This was a retrospective observational study. Between January 2011 and December 2016, 64 maintenance HD patients with newly developed pneumonia were admitted to Nagano Red Cross Hospital and all of them were enrolled in the study. The study protocol was approved by the institutional review board of the ethical committee at Nagano Red Cross Hospital and was conducted in accordance with the principles contained within the Declaration of Helsinki as revised in 2013.

Definitions

Pneumonia was defined as the presence of newly developed infiltration on chest X-ray and/or computed tomography and an increase in serum markers of inflammation (C-reactive protein >0.3 mg/dL and/or white blood cell count >10,000/µL). History of cardiovascular disease included angina pectoris, acute myocardial infarction, cerebral hemorrhage, cerebral infarction, peripheral arterial disease, and aortic dissection. History of malignancy included solid tumors, such as colon cancer and gastric cancer, and hematological malignancies, such as lymphoma and myeloma. Chronic lung disease was defined as the presence of chronic obstructive pulmonary disease or interstitial pulmonary disease. Disorientation was evaluated as altered mentality. Altered mentality was defined as a decrease in Japan Coma Scale score. Hypoxia was defined as patients who could not maintain an oxygen saturation level greater than 90% without supplemental oxygen supply. The presence of infiltrates in two or more lobes on chest X-ray and/or computed tomography was defined as multi-lobar lesions. The severity of pneumonia was evaluated using A-DROP score (age [male >70, female >75], dehydration, respiratory failure, orientation disturbance, and low blood pressure) [10]. In general, the dehydration section of the A-DROP scoring system is defined by blood urea nitrogen and physiological findings. In the current study, because our participants were HD patients, we excluded the dehydration section. Briefly, we defined the A-DROP score without including the dehydration section as the modified A-DROP score. The modified A-DROP score provided values of 0 to 4. Blood culture examinations were obtained within 24 h from admission and before the start of antibiotic therapy. Blood culture examinations were performed on either one or two sets. Clinical outcomes were defined as all-cause mortality within 30 days of hospital admission, clinical success of antibiotic therapy, duration of antibiotic therapy, and hospital mortality. Clinical success meant that pneumonia was successfully treated with the antibiotic selected at admission and that antibiotic was not changed except for the purpose of de-escalation. Failure of treatment was defined as death or a change in antibiotic from the initial therapy.

Statistical analysis

Continuous variables between the two groups were compared using the Mann-Whitney U test, and categorical variables were compared using Fisher's exact probability test. Continuous variables among three groups were compared using the Kruskal-Wallis test, and multiple comparisons between two groups were compared using the Mann-Whitney U test with Bonferroni correction. Factors associated with the clinical outcomes were analyzed using logistic regression analyses. The discriminatory ability of the factors was evaluated using the area under the receiver operating characteristic curve (AUC) analysis. A p value <0.05 was considered statistically significant. Analyses were performed using EZR (Saitama Medical Center, Jichi Medical University, Saitama, Japan), which is a graphical user interface for R (the R Foundation for Statistical Computing, Vienna, Austria) [12].

Results

Patient characteristics

The clinical characteristics of all 64 patients are shown in Table 1. The median age was 75 years. Forty-seven patients were male and 17 female. The main cause of HD was diabetic nephropathy (27 patients, 42.2%). Arteriovenous fistula or arteriovenous graft was the main type of vascular access. Thirty-four patients (53.1%) had cardiovascular disease complications, 21 (32.8%) had altered mentality, and 45 (70.3%) had hypoxia. Blood culture examinations were performed for 47 patients (73.4%), and three patients (6.4%) were positive. Fortytwo patients (65.6%) had multi-lobar lung infiltration, and 43 patients (67.2%) had pleural effusion. The severities of pneumonia evaluated using the modified A-DROP score were eight patients (12.5%) scored 0, 19 (29.7%) scored 1, 22 (34.4%) scored 2, 13 (20.3%) scored 3, and two (3.1%) scored 4. Nine patients (14.1%) died within 30 days of hospitalization, and 11 patients (17.2%) died in the all hospitalization period.

 Table 1
 Background clinical data and characteristics of all patients

Clinical characteristics		
Age (years)	75	37–88
Male (n, %)	47	73.4
BMI (kg/m²)	20.3	14.3-40.9
Duration of HD (months)	40	1–290
Cause of HD		
DMN (n, %)	27	42.2
Chronic GN (n, %)	21	32.8
Nephrosclerosis (n, %)	10	15.7
RPGN (n, %)	4	6.2
Other (<i>n</i> , %)	2	3.1
Vascular access		
AVF (n, %)	42	65.6
AVG (n, %)	15	23.5
Catheter (n, %)	7	10.9
Comorbidity		
CVD (n, %)	34	53.1
Malignancy (n, %)	12	18.8
CLD (n, %)	13	20.3
Vital signs		
Systolic BP (mmHg)	138	68–204
Diastolic BP (mmHg)	70	40-141
Heart rate (/min)	95	58-142
Altered mentality (n, %)	21	32.8
Fever (degree)	37.6	35.0-39.6
Hypoxia (n, %)	45	70.3
Blood examination		
Alb (g/dL)	3.1	2.0-4.3
BUN (mg/dL)	36.6	12.9-84.5
Cr (mg/dL)	5.49	1.48–13.32
Na (mEq/L)	139	129–147
K (mEq/L)	4.3	2.9-8.4
CRP (mg/dL)	8.2	0.9-43.1
WBC (/µL)	9590	3130-33520
Hb (g/dL)	10.7	4.1-16.5
Plt (×10 ⁴ /µL)	15.6	2.1-72.0
Bacterial cultures		
Sputum (<i>n</i> , %)	54	84.4
Blood (n, %)	47	73.4
Radiological findings		
Multi-lobar lesion (n, %)	42	65.6
Pleural effusion (n, %)	43	67.2

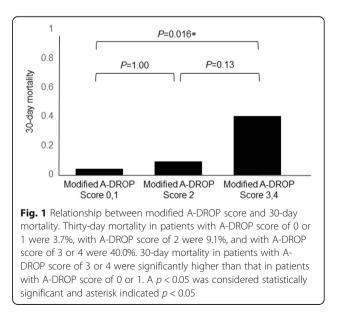
 Table 1
 Background clinical data and characteristics of all patients (Continued)

-		
Severity of pneumonia		
Modified A-DROP		
0 (n, %)	8	12.5
1 (n, %)	19	29.7
2 (n, %)	22	34.4
3 (n, %)	13	20.3
4 (n, %)	2	3.1
Therapy and prognosis		
Success of initial therapy (n, %)	46	71.9
Duration of antibiotics (days)	11	1–43
30-day mortality (<i>n</i> , %)	9	14.1
Hospital mortality (n, %)	11	17.2

Data for continuous variables are expressed as median and range, and categorical variables are expressed as number and percentage *Alb* albumin, *AVF* arteriovenous fistula, *AVG* arteriovenous graft, *BMI* body mass index, *BP* blood pressure, *BUN* blood urea nitrogen, *CLD* chronic lung diseases, *Cr* creatinine, *CRP* C-reactive protein, *CVD* cardiovascular disease, *DMN* diabetes mellitus nephropathy, *K* potassium, *Na* sodium, *GN* glomerulonephritis, *HD* hemodialysis, *Hb* hemoglobin, *PIt* platelet, *RPGN* rapid progressive glomerunephritis, *WBC* white blood cell count

Severity of pneumonia and clinical outcomes

One patient (3.7%) with a modified A-DROP score of 0 or 1 died, two patients (9.1%) with a modified A-DROP score of 2 died, and six patients (40.0%) with a modified A-DROP score of 3 or 4 died within 30 days of hospitalization (Fig. 1). Forty-six patients (71.9%) were successfully treated with initial antibiotic therapy. The median duration of antibiotic therapy was 11 days. The clinical characteristics among the three groups (modified A-DROP score 0 or 1, 2 or 3, or 4) is shown in Table 2.



WBC Hb (g/dL)

Plt (x $10^4/\mu$ L)

Bacterial cultures Sputum (*n*, %)

Blood (n, %)

Radiological findings Multi-lobar lesion (n, %)

Pleural effusion (n, %)

Severity of pneumonia	Modified		Modified		Modified		
	A-DROP 0, 1 n = 27		A-DROP		A-DROP		
			2		3, 4		p value
			n = 22		n = 15		
Age (years)	65	37–81	76	59–88	81	74–88	<0.001***
Male (n, %)	16	59.3	19	86.4	12	80.0	0.09
BMI (kg/m²)	20.7	16.1-40.9	19.4	14.3–26.3	20.4	14.8–23.9	0.66
Duration of HD (months)	47	3-231	37	2-290	48	1-154	0.97
Cause of HD							
DMN (<i>n</i> , %)	8	29.7	12	54.6	7	46.7	0.20
Chronic GN (n, %)	10	37.0	6	27.3	5	33.3	0.75
Nephrosclerosis (n, %)	5	18.5	2	9.1	3	20.0	0.62
RPGN (n, %)	3	11.1	1	4.5	0	0	0.54
Other (<i>n</i> , %)	1	3.7	1	4.5	0	0	1.00
Vascular access							
AVF (n, %)	21	77.8	13	59.1	8	53.3	0.21
AVG (n, %)	3	11.1	8	36.4	4	26.7	0.10
Catheter (n, %)	3	11.1	1	4.5	3	20.0	0.40
Comorbidity							
CVD (n, %)	13	48.1	10	45.5	11	73.3	0.23
Malignancy (<i>n</i> , %)	4	14.8	4	18.2	4	26.7	0.65
CLD (n, %)	6	22.2	5	22.7	2	13.3	0.85
Vital signs							
Systolic BP (mmHg)	129	88–204	150	97–170	120	68–203	0.18
Diastolic BP (mmHg)	74	53–103	72	47-141	64	40–99	0.24
Heart rate (/min)	98	68–142	96	68–136	94	58–130	0.49
Altered mentality (n, %)	0	0	7	31.8	14	93.3	<0.001***
Fever (degree)	37.1	35.5–39.6	37.7	35.0-39.3	37.8	36.1–39.3	0.38
Hypoxia (n, %)	11	40.7	19	86.4	15	100	<0.001***
Blood examination							
Alb (g/dL)	3.1	2.1-4.1	3.3	2.1-4.3	3.0	2.0-3.9	0.39
BUN (mg/dL)	35.2	13.2-80.7	39.4	12.9–84.5	34.2	13.6–74.3	0.48
Cr (mg/dL)	5.99	1.48–13.32	5.23	2.10-13.05	5.25	2.65-11.20	0.26
Na (mEq/L)	138	129–145	140	132–147	140	131–147	0.11
K (mEq/L)	4.2	3.2-5.9	4.5	3.5–8.2	4.1	2.9–8.4	0.25
CRP (mg/dL)	7.91	1.21-30.80	9.16	0.85-43.12	9.54	1.37-13.99	0.98
WBC (/µL)	9600	4220-23100	9910	3130-33520	9580	3600-28910	0.99

Table

10.6

16.2

20

17

15

14

4.1-16.5

2.7-50.0

74.1

63.0

55.6

51.9

10.9

17.6

20

20

15

15

7.6-14.4

2.1-31.3

90.9

90.9

68.2

68.2

10.5

14.4

14

10

12

14

7.1-13.5

6.8-72.0

93.3

66.7

80.0

93.3

0.98

0.88

0.22

0.07

0.26

0.012*

			each group (Co	Shtinuea)			
Therapy and prognosis							
Success of initial therapy							
(n, %)	21	77.8	17	77.3	8	53.3	0.22
Duration of antibiotics							
(days)	8	1–43	12	3–36	13	3–36	0.023*
30-day mortality (n, %)	1	3.7	2	9.1	6	40.0	0.004**
Hospital mortality (n, %)	1	3.7	3	13.6	7	46.7	0.003**

 Table 2 Background clinical data and characteristics of each group (Continued)

Data for continuous variables are expressed as median and range, and categorical variables are expressed as number and percentages. Categorical variables were compared using Fisher's exact probability test, and continuous variables among three groups were compared using the Kruskal–Wallis test. Significant difference are indicated with asterisks (***p < 0.001, **p < 0.001, *p < 0.05)

Alb albumin, AVF arteriovenous fistula, AVG arteriovenous graft, BMI body mass index, BP blood pressure, BUN blood urea nitrogen, CLD chronic lung diseases, Cr creatinine, CRP C-reactive protein, CVD cardiovascular diseases, DMN diabetes mellitus nephropathy, K potassium, Na sodium, GN glomerulonephritis, HD hemodialysis, Hb hemoglobin, Plt platelet, RPGN rapid progressive glomerulonephritis, WBC white blood cell count

Age, altered mentality, hypoxia, pleural effusion, duration of antibiotic therapy, 30-day mortality, and hospital mortality were significantly different among the three groups. Logistic regression analysis showed that the modified A-DROP score was significantly associated with 30-day mortality (Table 3). The discriminatory ability of the modified A-DROP score was assessed using AUC analysis (AUC 0.810; 95%CI 0.653–0.967; p < 0.01) (Fig. 2).

Bacteria and antibiotic therapy

 α -Streptococcus, Candida, Neisseria, and S. aureus were the main pathogens detected in sputum cultures, while Streptococcus pneumoniae and Branhamella catarrhalis were detected in a few cases only (Table 4). Klebsiella pneumoniae was detected in two patients and S. pneumoniae was detected in one patient from blood cultures. Ampicillin/sulbactam, tazobactam/piperacillin, and meropenem were the main initial antibiotic therapies (Table 5).

Discussion

Previous studies have reported hospital mortality from pneumonia in HD patients as 12.4% and 30-day mortality as 11.6% [1, 13]. In the current study, 30-day mortality was 14.1% and prognosis was similar as the previous studies. A previous study compared the prognosis between HD patients with pneumonia and patients with HCAP and did not find a significant difference [7]. In addition, the bacteria causing pneumonia in HD patients

 Table 3 Association between 30-day mortality and modified

 A-DROP score

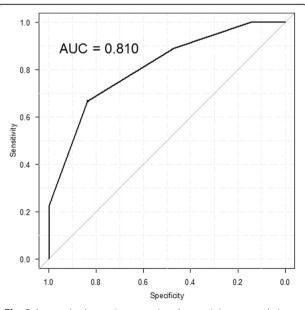
	OR	CI	p value
Modified A-DROP	4.67	1.63–13.3	0.004**

Logistic regression analysis reveals the association between 30-day mortality and modified A-DROP score. Significant difference are indicated with asterisks (**p < 0.01)

Cl confidence interval, OR odds ratio

and HCAP are similar. Thus, the clinical characteristics between the two groups are similar.

When predicting the prognosis of pneumonia or evaluating the severity of pneumonia, either the PSI, CURB65, or A-DROP scoring systems are used. However, these scoring systems include blood urea nitrogen, dehydration, or pleural effusion [8–10], which are strongly influenced by renal impairment and dialysis. This means that it is difficult to accurately evaluate the severity of pneumonia in dialysis patients. In such patients, the severity of pneumonia should be evaluated using a scoring system that excludes those factors associated with kidney function or dialysis.



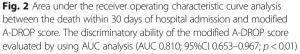


Table 4 Type of bacteria isolated from sputum cultures

Type of bacteria	n
a-Streptococcus spp.	35
Candida spp.	35
Neisseria spp.	20
Staphylococcus aureus (including MRSA)	17
Haemophilus parainfluenzae	8
Corynebacterium spp.	7
Klebsiella oxytoca	6
Escherichia coli (including ESBL-producing E. coli)	6
Staphylococcus epidermidis	5
Klebsiella pneumoniae	3
Pseudomonas aeruginosa	3
Branhamella catarrhalis	2
Serratia marcescens	1
Streptococcus pneumoniae	1
Streptococcus agalactiae	1
Acinetobacter baumannii	1
Enterobacter	1
Citrobacter spp.	1

ESBL extended spectrum beta-lactamase, MRSA methicillin-resistan Staphylococcus aureus, Spp species

In the current study, we used the A-DROP scoring system but excluded the dehydration section to evaluate the severity of pneumonia in HD patients. The modified A-DROP score was found to be significantly associated with prognosis in HD patients with pneumonia. It is suggested that the modified A-DROP score is useful for evaluating the severity of pneumonia in HD patients. A benefit of this system is that clinical data (age, blood pressure, orientation, and hypoxia) are easy to obtain and do not require blood examinations. In short, the modified A-DROP score is a good and convenient option not only in hospitals but also in HD clinics.

With regard to the bacteria isolated from sputum cultures, gram-positive coccus such as α -Streptococcus and *S. aureus* were the main species detected. *S. pneumoniae* and *B. catarrhalis* are often detected in non-HD patients presenting with pneumonia [14, 15]. A previous study by Kawasaki et al. reported that *S. pneumonia* is the second most frequently detected pathogen in HD patients with pneumonia [13]. However, *S. pneumonia* and *B. catarrhalis* were detected in only a few cases. Most patients were elderly and some presented with dysphagia and might develop aspiration pneumonia. Therefore, the detected bacteria were not *S. pneumonia* or *B. catarrhalis* but indigenous bacterium of the oral cavity such as α -Streptococcus.

This study examined HD patients, who have an increased risk for blood stream infections; however, there

ру

Initial antibiotic therapy	n
ABPC/SBT	16
ABPC/SBT + CPFX	4
ABPC/SBT + LVFX	1
TAZ/PIPC	8
TAZ/PIPC + LZD	1
CMZ	1
CTRX	4
CTRX + CLDM	3
CPZ/SBT	1
CPZ/SBT + AZM	1
CFPM	1
CFPM + CLDM	1
BIPM	1
MEPM	10
MEPM + CPFX	1
MEPM + PZFX	1
MEPM + LZD	1
DRPM + TEIC	1
AZM	1
AZT + VCM	1
PZFX	4
LVFX	1

ABPC/SBT ampicillin/sulbactam, AZM azithromycin, AZT aztreonam, BIPM biapenem, CFPM cefepime, CLDM clindamycin, CMZ cefmetazole, CPFX ciprofloxacin, CPZ/SBT cefoperazone/sulbactam, CTRX cefriaxone, DRPM doripenem, LVFX levofloxacin, LZD linezolid, MEPM meropenem, PZFX pazufloxacin, TAZ/PIPC tazobactam/piperacillin, TEIC teicoplanin, VCM vancomycin

were only three patients (6.4%) with positive blood cultures. A previous study of non-HD patients with pneumonia reported a positive blood culture rate of 5.7%, and it was not associated with the severity of pneumonia evaluated using PSI [16]. These results suggest that blood culture examination is not useful for detecting the causative microorganism in patients with bacterial pneumonia. Recently, routine blood culture examinations have been not recommended for patients presenting with pneumonia [17].

This study had some limitations. We could not fully evaluate the severity of pneumonia using CURB65 or PSI. Because we could not obtain data for respiration rates, we evaluated the severity of pneumonia using the modified A-DROP score. Although smoking is a risk factor for community-acquired pneumonia [18], we were unable to obtain patient smoking histories. Bedridden patients or patients with dysphagia often have repeated aspiration pneumonia and have a poor prognosis, and activities of daily living and cognitive impairment are important for the prognosis of pneumonia [19]. However, we could not obtain data about patients' activities of daily living or cognitive function. Although this study had a small sample size, we collected and analyzed clinical data such as the severity of pneumonia and prognosis, duration of antibiotic therapy, and success of initial therapy in details. We could not diagnose whether a patient had aspiration pneumonia as it is difficult to correctly diagnose if a patient presenting with pneumonia has aspiration pneumonia. Because information of the quality of sputum could not be obtained, some sputum samples mainly contained salivary contents, resulting detecting indigenous bacterium of the oral cavity.

We could not unify the timing of evaluation of the modified A-DROP score in the current study. Therefore, we examined when the modified A-DROP score was evaluated. According to the timing of HD sessions, we divided the timing of the modified A-DROP score evaluation into three groups: (1) before HD sessions, (2) between HD sessions, and (3) after HD sessions. Eighteen patients were evaluated for the modified A-DROP score before HD sessions, 25 were evaluated between HD sessions, and 21 were evaluated after HD sessions. Because it is possible that blood pressure, fluid volume, and hypoxia can change depending on the timing of a HD session, and this can influence the evaluation of the A-DROP score (as well as the modified A-DROP score being influenced by when the modified A-DROP score was evaluated), we compared the frequency of the modified A-DROP score among the three groups (before HD sessions, between HD sessions, and after HD sessions). As a result, the frequency of the modified A-DROP score was not significantly different among the groups (Additional file 1: Table S1). However, not unifying the timing of evaluation of the modified A-DROP score is a limitation of the current study.

Conclusions

In conclusion, the modified A-DROP score reflected the severity of pneumonia and was significantly associated with 30-day mortality in this population of HD patients. Patients with a modified A-DROP score of 3 or 4 had a poor prognosis.

Additional file

Additional file 1: Table S1. Relationships between the timing of evaluating modified A-DROP score and modified A-DROP score. (DOCX 14 kb)

Abbreviations

AUC: Area under the receiver operating characteristic curve; HCAP: Healthcare-associated pneumonia; HD: Hemodialysis; PSI: Pneumonia severity index

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Availability of data and materials Please contact with the corresponding author for data requests.

Authors' contributions

MH, KF, and YK designed the study and collected the data. MH and TI wrote the manuscript. TM and MK corrected the manuscript, tables, and figures. All authors read and approved the final manuscript.

Ethics approval and consent to participate

The study protocol was approved by the institutional review board of the ethical committee at Nagano Red Cross Hospital and was conducted in accordance with the principles contained within the Declaration of Helsinki as revised in 2013.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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Author details

¹Department of Nephrology, Nagano Red Cross Hospital, 5-22-1, Wakasato, Nagano 380-8582, Japan. ²Department of Nephrology, Shinshu University School of Medicine, 3-1-1, Asahi, Matsumoto 390-8621, Japan. ³Department of Infection and Host Defense, Nagano Red Cross Hospital, 5-22-1, Wakasato, Nagano 380-8582, Japan. ⁴Department of Respiratory Medicine, Nagano Red Cross Hospital, 5-22-1, Wakasato, Nagano 380-8582, Japan.

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