Developing and validating a multivariable prediction model for in-hospital mortality of pneumonia with advanced chronic kidney disease patients: a retrospective analysis using a nationwide database in Japan

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Abstract

Background:

The prognosis of pneumonia in patients with advanced stage chronic kidney disease (CKD) remains unimproved for years. We attempt to develop a simple and more useful scoring system for predicting in-hospital mortality for advanced CKD patients with pneumonia.

Methods:

Using the Diagnosis Procedure Combination database, we identified the in-hospital adult patients both with a record of pneumonia and stage 5 or 5D CKD as a comorbidity on admission between April 1, 2012 and March 31, 2016. Predictive variable selection was analyzed by multivariable logistic regression analysis, stepwise method, LASSO method and random forest method, and then develop a new simple scoring system seeking for highest c-statistics combination of variables in one sample dataset for model development. Finally, we compared c-statistics of univariate logistic regression about new scoring system with c-statistics about "A-DROP" in the other sample dataset.

Result:

We identified 8,402 patients in 707 hospitals, and the total in-hospital mortality was 11.0% (437 patients) in development dataset. Seven variables were selected, which includes age (male ≥ 70 years, female ≥ 75 years), respiratory failure, orientation disturbance, low blood pressure, the need of assistance in feeding or bowel control, severe or moderate thinness and CRP 200 mg/L or extent of consolidation on chest X-ray

≥2/3 of one lung. The c-statistics of univariate logistic regression was 0.8017 using seven variables, while that was 0.7372 using "A-DROP"

Conclusion:

In advanced CKD patients, if we select appropriate variables for predicting in-hospital mortality, simple scoring system may have better discrimination than "A-DROP".

Introduction

The prognosis of pneumonia in patients with advanced stage chronic kidney disease (CKD) has been poorer than that in the general population, and remains unimproved for years [1-3]. Compared with patients with normal renal function, the adjusted hazard ratio for hospitalization with pneumonia in CKD patients with an estimated glomerular filtration rate less than 30 ml/min/1.73m^2 was 15, and the incidence of death within 30 days of hospitalization with pneumonia was about 12 times higher [1]. In cases of hemodialysis patients, the mortality rate due to infectious disease remained unchanged from 1988 to 2013, while the mortality rate due to other diseases such as cardiovascular disease tended to decrease each year [2]. The fact that pneumonia accounted for 46.1% of all deaths from infectious disease in hemodialysis patients [4] suggests that pneumonia could be a critical illness in advanced CKD patients.

The first step to treat pneumonia in advanced CKD patients is the assessment of the degree of the disease's severity. Currently, "CURB-65" is utilized as one of the most useful severity scores [5], and "A-DROP" was modified from "CURB-65" by the Japanese Respiratory Society [6]. The "A-DROP" scoring system, which is a 6-point scale (0–5) to assess the clinical severity of community acquired pneumonia, assesses the following parameters: (i) age (male ≥70 years, female ≥75 years); (ii) dehydration (blood urea nitrogen (BUN) ≥210 mg/L); (iii) respiratory failure (arterial oxygen saturation (SpO2) ≤90% or partial pressure of oxygen in arterial blood (PaO2) ≤60 mmHg); (iv) orientation disturbance (confusion); and (v) low blood pressure (systolic blood pressure (SBP) ≤90 mmHg). However, "A-DROP" is not always suitable for assessing the severity of pneumonia in patients with advanced CKD. An increase in BUN is used to detect the presence of dehydration in “CURB-65” and “A-DROP”, and can be an important factor affecting the patient’s mortality; however, BUN is often high in patients with advanced CKD even when they are not dehydrated, so an elevated BUN would not be a good marker for the evaluation of pneumonia in advanced CKD patients. Given these facts, other scores that reflect the severity of pneumonia will be required in order to assess the severity of pneumonia in CKD patients. Accordingly, serum C-reactive protein (CRP) or body mass index might be other candidates as a better marker [7].

In this article, we attempt to develop a more useful and simple scoring system than “A-DROP” for adequately predicting in-hospital mortality for advanced CKD patients with pneumonia.

Methods

Data source

We retrospectively analyzed a nationwide administrative database in Japanese acute care hospitals. In brief, Japan operates a public health care payment system, Diagnosis Procedure Combination (DPC)/Per-Diem Payment System (PDPS) [8], which is currently used by more than 80% of acute care hospitals. In this study, we were able to utilize about 70% of DPC data for analysis. Interestingly, DPC data includes important clinical factors, such as clinical summaries and severity of pneumonia upon admission. The International Classification of Diseases, 10th Revision (ICD-10) codes were used for diagnosis in the DPC data. A previous paper documenting that the DPC dataset had strong predictive power for in-hospital mortality in CAP patients indicated these data were clinically reliable [7].

Inclusion and exclusion criteria of participants

Figure 1 illustrates the process for patient selection. The following were inclusion criteria: (i) in-hospital patients with a record of pneumonia (J10.0, J11.0, J12–18, A48.1, B01.2, B05.2, B37.1, or B59 in the 2003 version of the ICD-10) in both the trigger and principle diagnoses between April 1, 2012 and March 31, 2016; (ii) patients with a record of end stage renal disease (ESRD) or stage 5 or 5D CKD (N18.0 in the 2003 version of the ICD-10) as advanced CKD on admission; and (iii) those aged from 18 to 94 years. In contrast, patients who received renal transplantation and those who had missing data about baseline variables were excluded from this study (complete case analysis).

Baseline variables

We analyzed patient age, sex, body mass index (BMI), the components of Barthel index (independence of feeding, bathing, grooming, dressing, bowels, bladder, toilet use, transfers from bed to chair, mobility on level surfaces, stairs), orientation disturbance due to pneumonia, BUN ≥210 mg/L or dehydration, SpO_2 <90%, SBP <90 mmHg [6], C-reactive protein (CRP) level (over 200 mg/L) or the extent of consolidation on chest radiography (≥2/3 of one lung) [9], maintenance hemodialysis or peritoneal dialysis as renal replacement therapies, ambulance use, hospitalization within 90 days at the same hospital, and comorbidities upon admission, including diabetes, cancers, heart diseases (congestive heart failure and/or old myocardial infarction), cerebrovascular disease, and liver disease [7]. All covariates were detected on admission and the cut-off-values were referenced from past researches.

The patients were classified into 8 groups based on age (<65 years, 65–70, 70–74, 75–80, 80–84, 85–90, 90–95, and ≥95 years) and into four groups based on BMI (<17 kg/m^2, severe or moderate thinness; 17–18.5 kg/m^2, mild thinness; 18.5–25 kg/m^2, normal range; and ≥25 kg/m^2, overweight) according to the guidelines of the World Health Organization [10]. The participants were classified into two categories by arterial oxygen saturation (<90% or ≥90%), SBP (<90 mmHg or ≥90 mmHg), and orientation disturbance and dependence of activities of daily living (ADL) according to the components of the Barthel index score (independent or dependent on each component) [11]. Maintenance hemodialysis and peritoneal dialysis were not on the DPC data, so we used these two variables based on the claim codes for dialysis and no diagnosis of acute kidney injury [12].

Statistical analyses

As shown in Figure 2, we first divided participants into two groups in order to evaluate the performance of the model using other participant data after developing a prediction model. One group included patients who were admitted between April 1, 2012 and March 31, 2015 and were analyzed as a training dataset to develop a prediction model, and the other included those who were admitted between April 1, 2015 and March 31, 2016, to be validated as a test dataset.

In the present study, the primary outcome was all-cause in-hospital mortality. The training dataset was analyzed using multivariate logistic regression analysis on age, sex, BMI, the components of the Barthel index [11], orientation disturbance, SpO2, SBP, CRP level (over 200 mg/L) or the extent of consolidation on chest radiography (≥2/3 of one lung) upon admission, ambulance use, hospitalization within 90 days at the same hospital, and comorbidities upon admission, as previously categorized in the section regarding baseline variables. The comorbidities include diabetes, cancers, heart diseases, cerebrovascular disease, and liver disease. In order to ensure the robustness of our variables selection, we analyzed the data using four different kinds of mathematical models. The 1st model involved multivariable logistic regression analysis using all the variables above. The 2nd model contained stepwise selection models with forward and backward methods that applied the Akaike Information Criterion (AIC) with R package "MASS" [13]. The 3rd model included least absolute shrinkage and selection operator (LASSO) penalization with R package "glmnet", which is a shrinkage regression technique recommended for predicting regression models with many predictor variables [14, 15]. In detail, we rescaled the continuous variables into the dummies as noted above, standardized all the binary covariates including the dummies, and determined the penalty parameter by 10-fold cross-validation. The 4th model involved the random forest method with R package "randomForest", which is used as a nonparametric regression for building a predictor ensemble with a set of decision trees, and we can measure the importance of each variable [16-18]. The number of variables randomly sampled as candidates at each point in the 4th model was the square root of the number of variables. The variable importance measures were produced with a mean decrease in node impurity, which was measured by the Gini impurity (MDG) [18, 19]. Subsequently, we selected important variables fulfilling all the required conditions: (i) a significant difference in the 1st model; (ii) not dropped in the 2nd and 3rd models; and (iii) MDG value was the median or more in the 4th model. Next, we developed a new, simple scoring system using one ordered categorical variable, which was the sum of each score with the selected variables to predict in-hospital mortality, seeking the highest C-statistic in all the kinds of combinations of candidates newly founded. We reconstructed the two variables divided in variable selection to compare “A-DROP” with the new scoring system as follows: age was classified into two categories (male ≤70 years, female ≤75 years) like "A-DROP", and ADL was also integrated into two categories (independent or dependent on each selected component of Barthel index.

Finally, we analyzed the test dataset using univariate logistic regression and confirmed the predictive performance not only by discrimination using the area under curve (AUC) of the receiver operating characteristic (ROC) curve but also by calibration using a calibration plot.

A sensitivity analysis was executed to confirm the performance of the new scoring system for patients who lived longer in hospitals. We restricted the analysis to patients whose length of stay was more than 2, 3, and 4 days.

Sample size was calculated by event per variable for logistic regression after we excluded the missing data[20]. A two-sided significance level of 0.05 was used, and all analyses were conducted using R version 3.4.1 (The R Development Core Team, Vienna, Austria).

Results

The DPC database documented a total of 707 hospitals and 8,402 patients with ESRD who were admitted due to pneumonia. After 2,805 patients were excluded due to missing data, the remaining 5,597 were divided into training data (3,967) and test data (1,630) (Fig 1). The summary of the baseline characteristics and an outcome of the patients in the training and test datasets were shown in Table 1. It was found that the total in-hospital mortality was 11.0% (437 patients), and BUN ≥210 mg/L or dehydration was 76.7% in the training dataset.

Variable selections in training data

Results of the multivariate analysis of in-hospital mortality in four models are reported in Table.2. Among the components of "A-DROP", age, low arterial oxygen saturation, low SBP, and orientation disturbance due to pneumonia were selected as important variables, but BUN ≥210 mg/L or dehydration was not selected in each model. On the other hand, maintenance hemodialysis, the need for assistance with feeding and bowel control, which were components of ADL severe or moderate thinness (BMI <17 kg/m^2), CRP

200 mg/L or extent of consolidation on chest X-ray ≥2/3 of one lung, and recent hospitalization within 90 days were selected as important variables. Then, we added the variables to the components of “A-DROP without dehydration” in all combinations of variables (Table 3). The highest C-statistic was 0.8069, and the unique components were the following three: the need for assistance with feeding or bowel control, severe or moderate thinness, and CRP 200 mg/L or extent of consolidation on chest X-ray ≥2/3 of one lung. In addition, we made a “new score” with a total of seven binary variables (these three new variables and “A-DROP without dehydration”).

Validation using test data

Results of discrimination with an ROC curve, comparing the “new score”, “A-DROP without dehydration”, and “A-DROP” using univariate logistic analysis in the test dataset are depicted in Figure 3. In our test dataset, the C-statistics were 0.8017 (95% confidence interval (CI); 0.7711-0.8324) about “new score”, 0.7565 (95% CI; 0.7230-0.7899) about “A-DROP without dehydration”, and 0.7372 (95% CI; 0.7005-0.7740) about “A-DROP”. When we restricted the analysis to patients whose length of stay was more than 2 days, the C-statistic of the new scoring system was 0.7995; more than 3 days: 0.7918; more than 4 days: 0.7835.

Results of validation with a calibration plot, essentially, the comparison of proportion in the training set with that in the test set for each score are represented in Figure 4. The new score could predict each in-hospital mortality and classify the severity, especially in the case of low probability.

Sensitivity and specificity of each score are shown in Table 4. A score ≥3 achieved a sensitivity of 70.6% and specificity of 73.7% in prediction of in-hospital mortality.

Discussion

In the current study of 707 acute care hospitals, we identify a novel and simple scoring system that could predict in-hospital mortality in stage 5 or 5D CKD patients with pneumonia. We found that seven components were identified for the scoring system, including the combination age and sex, orientation disturbance, SpO2, SBP, the need for assistance with feeding or bowel control, BMI <17 kg/m^2, and CRP 200 mg/L or the extent of consolidation on chest X-ray ≥2/3 of one lung. The BUN ≥210 mg/L or hydration, which is one component of "A-DROP", was not selected in any model. Importantly, our system for calculating the sum of each score was useful in advanced CKD patients with pneumonia, and the AUC was improved in a test dataset and reached more than 0.8, implying "excellent discrimination" [21].

The "No Free Lunch Theorem" mentions that no universal search algorithm exists to solve all problems in statistics [22], implying that one mathematical method alone would not be sufficient enough to lead to a conclusion, and using several analyses would lead to a better conclusion. In the present study, we utilized four different models to assess variable selection and found that these methods identified several clinical significances. It is noted that "either BUN ≥210 mg/L or dehydration" constantly failed to be of importance in all four different models, although this parameter was considered as an important clinical variable in “A-DROP”. An explanation could be that our study subjects were advanced CKD patients with pneumonia, so this parameter would not be suitable for predicting all-cause in-hospital mortality under such a unique condition. Moreover, the three additional variables enabled us to assess the severity of pneumonia more precisely than “A-DROP”. In clinical settings, when the severity of pneumonia under hemodialysis is regarded as a slight illness, we will sometimes treat pneumonia without hospital admission because hemodialysis patients usually attend hospital 3 times per week. Therefore, the higher performance of the new scoring system, including sensitivity and specificity, will contribute to deciding whether advanced CKD patients should be hospitalized.

In our scoring system, we decided to evaluate these additional three unique variables, including the need for assistance with feeding or bowel control as ADL dependence, BMI <17 kg/m^2, and CRP 200 mg/L or extent of consolidation on chest X-ray ≥2/3 of one lung. Importantly, we assumed that these three parameters are important, although these variables are not used in the “A-DROP” scoring system. This is because, first, ADL dependence was reported to be correlated with increased risk of mortality [23, 24]. Our analysis revealed that the need for assistance especially with feeding or bowel control was important for predicting in-hospital mortality. ADL is often classified into three factors: cognitive, motor, and perceptual abilities [25], and the need for assistance with feeding or bowel control could probably be classified as a cognitive ability, so other variables could not be replaced in our multivariable analysis. Moreover, feeding or bowel control seems to be a more sensitive marker in the later stages of dementia than dressing or bathing [26]. Therefore, we believed that feeding or bowel control revealed the severity of ADL dependencies and should be included in our prediction score.

Second, our study demonstrated that BMI <17 kg/m^2 (the WHO classified this as severe or moderate thinness [10]) was significantly associated with higher mortality, but obesity was not significant. Several studies have documented the existence of an "obesity survival paradox", in which obesity was negatively associated with mortality in the general population with pneumonia [27], whereas being underweight was positively associated with increased mortality [28]. A recent systematic review and meta-analysis showed that BMI (per 1 kg/m^2 increment) was associated with a reduced risk of all-cause mortality in patients undergoing hemodialysis [29]. Therefore, severe or moderate thinness would be associated with higher mortality in patients undergoing hemodialysis with pneumonia.

Third, CRP of 200 mg/L or consolidation on chest radiography was also found to be positively and significantly associated with in-hospital mortality in our study. These parameters are able to assess the severity of healthcare-associated pneumonia (HCAP) and are components of "I-ROAD", which is a prognostic tool for patients with HCAP [9]. Some patients with HCAP also had CKD stage 5D [30], so our results were consistent with previous reports. Given these results, we think that these three unique variables would reflect the progression of pneumonia in advanced CKD patients with pneumonia.

Limitations

Our study has some limitations. First, a critical issue as to whether the patients were on dialysis or not in the DPC database was not directly addressed. In our analysis, the information for hemodialysis or peritoneal dialysis was based on the claim codes, but not on clinical summaries in DPC data. If this information is taken into account, this variable might change our scoring system. However, our scoring system has already demonstrated better discrimination than “A-DROP”. Second, our data analysis did not include unmeasured variables, such as pneumococcal vaccine, the existence of drug-resistant bacteria, or some laboratory results, which might have influenced the outcome of our study. Finally, we performed a complete case analysis because of a lack of data, so this might have influenced variable selection. However, we performed an extended multiple imputation using the chained equations technique [31], and confirmed that there are not great difference between the result of complete case analysis and the result of it (data not shown).

Conclusion

We identified a novel, simple prediction model of in-hospital mortality in CKD 5 or 5D patients with pneumonia. Our model may provide better performance than “A-DROP” for predicting in-hospital mortality in CKD 5 or 5D patients. Our findings suggest that when predicting the in-hospital mortality of patients in an advanced stage of CKD, appropriate variables should be selected. Further studies are needed to confirm the availability of this model and its application for outpatients to evaluate the severity.

Compliance with Ethical Standards

The study protocol was approved by the ethics committee of Kyoto University Graduate School and the Faculty of Medicine (approval number: R0135). This study was conducted in accordance with the ethical guidelines for medical and health research involving human participants issued by the Japanese National Government. These guidelines include a stipulation for the protection of patient anonymity. The data were anonymized, and the requirement for informed consent was waived.

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Authors contribution:

Research idea and study design: DT, SK, TM, MY, YI; data analysis/interpretation: DT, SK, YI; data acquisition: DT, SK, KF, YI; statistical analysis: DT, YI. Each author contributed important intellectual content during manuscript drafting or revision, accepts personal accountability for the author's own contributions, and agrees to ensure that questions pertaining to the accuracy or integrity of any portion of the work are appropriately investigated and resolved.

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Figure captions

Figure.1 Patient selection

Figure.2 Flow chart of analysis

First, we selected important variables fulfilling all the required conditions: (i) a significant difference in the 1st model; (ii) not dropped in the 2nd and 3rd models; and (iii) MDG value was the median or more in the 4th model. Next, we developed a new, simple scoring system using the sum of each score with the selected variables to predict in-hospital mortality, seeking the highest C-statistic in all the kinds of combinations of candidates newly founded. Finally, we analyzed the test dataset using univariate logistic regression and confirmed the predictive performance by discrimination using the area under curve (AUC) of the receiver operating characteristic (ROC) curve.

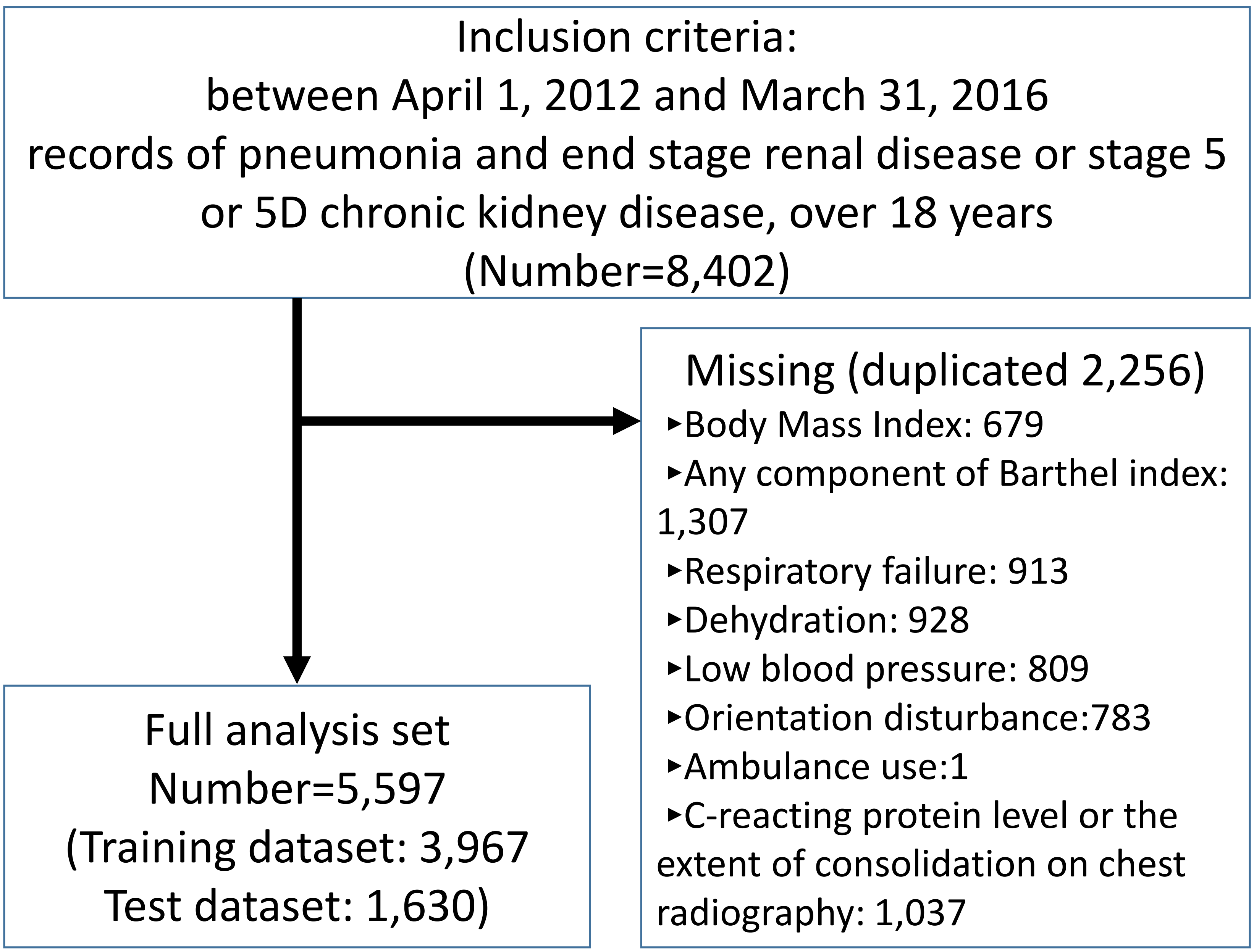
Figure.3 The results of discrimination with an ROC curve

We compared the "new score", "A-DROP without dehydration", and "A-DROP" using univariate logistic analysis in the test dataset.

Figure.4 The results of validation with a calibration plot

The new score could predict each mortality and classify the severity, especially in the case of low probability.

Figure.1



Inclusion criteria:
between April 1, 2012 and March 31, 2016
records of pneumonia and end stage renal disease or stage 5 or 5D chronic kidney disease, over 18 years
(Number=8,402)
Missing (duplicated 2,256)
►Body Mass Index: 679
►Any component of Barthel index: 1,307
►Respiratory failure: 913
►Dehydration: 928
►Low blood pressure: 809
►Orientation disturbance:783
►Ambulance use:1
►C-reacting protein level or the extent of consolidation on chest radiography: 1,037
Full analysis set
Number=5,597
(Training dataset: 3,967
Test dataset: 1,630)

Figure.2

In training dataset (development)

Selected variables according to past papers, including “A-DROP” (age (male ≥70 years, female ≥75 years), dehydration (blood urea nitrogen ≤210 mg/L), respiratory failure, orientation disturbance, low blood pressure)

4 steps of variable selection ***(Table.2)***

- ✓ Significant in logistic full model *(1st model)*
- ✓ Not dropped in stepwise model *(2nd model)*
- ✓ Not dropped in LASSO model *(3rd model)*
- ✓ Mean Decrease Gini is median or more in random forest model *(4th model)*

- **4 variables from “A-DROP”** (dropped dehydration)
- **5 new candidate variables** (receiving chronic hemodialysis, the need of assistance in feeding and bowel control, severe or moderate thinness (BMI <17 kg/m^2), CRP 200 mg/L or extent of consolidation on chest X-ray ≥2/3 of one lung and recent hospitalization within 90 days)

Evaluation of 5 unique candidates in addition to each component of “A-DROP without dehydration” to isolate the factor with highest c-statistics ***(Table.3)***

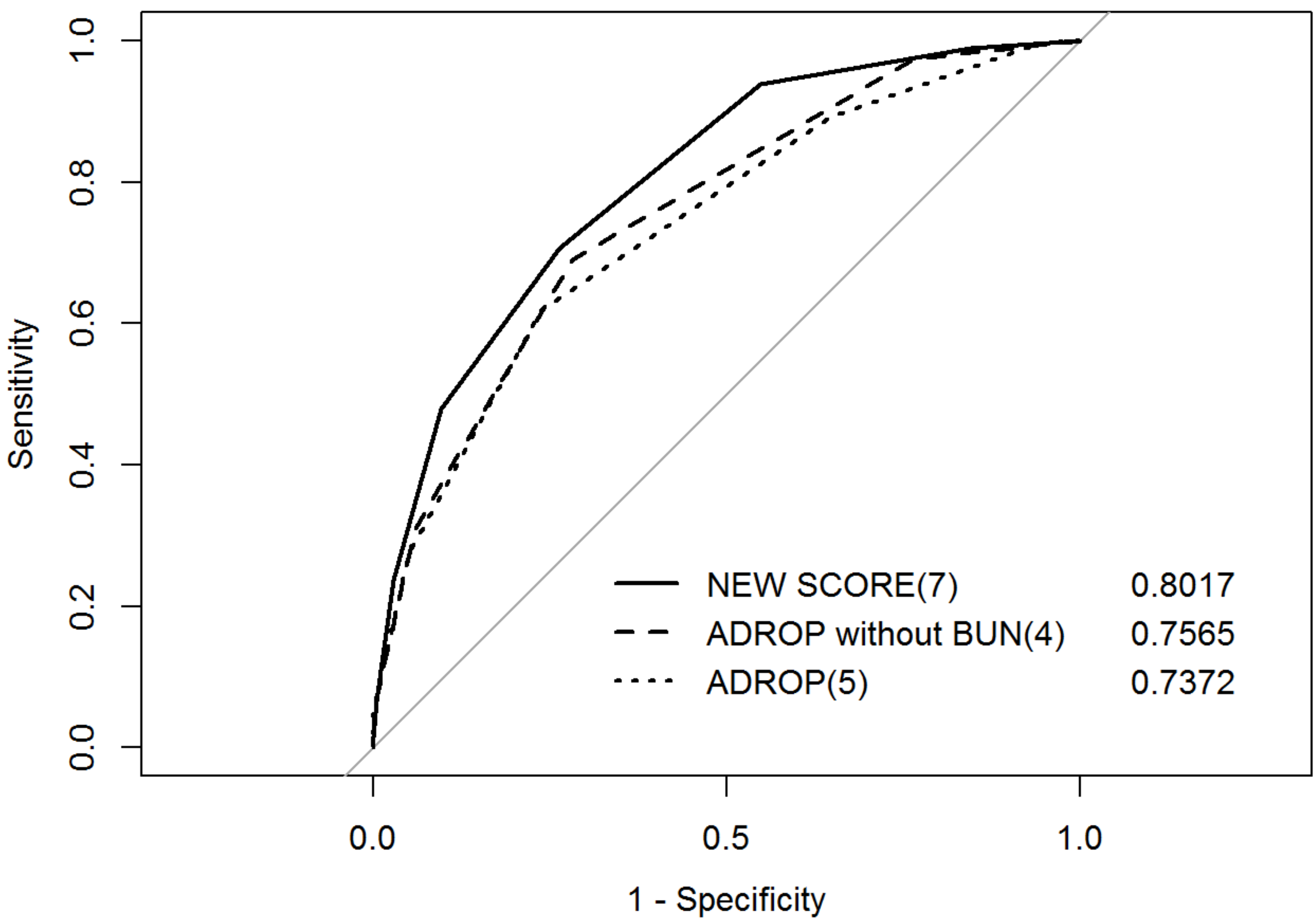
“New score” modified from “A-DROP” (the need of assistance in feeding or bowel control, severe or moderate thinness, CRP 200 mg/L or extent of consolidation on chest X-ray and the components of “A-DROP without dehydration”)

In test dataset (validation)

Validate each c-statistics of score in univariate analysis ***(Figure.3 & 4)***

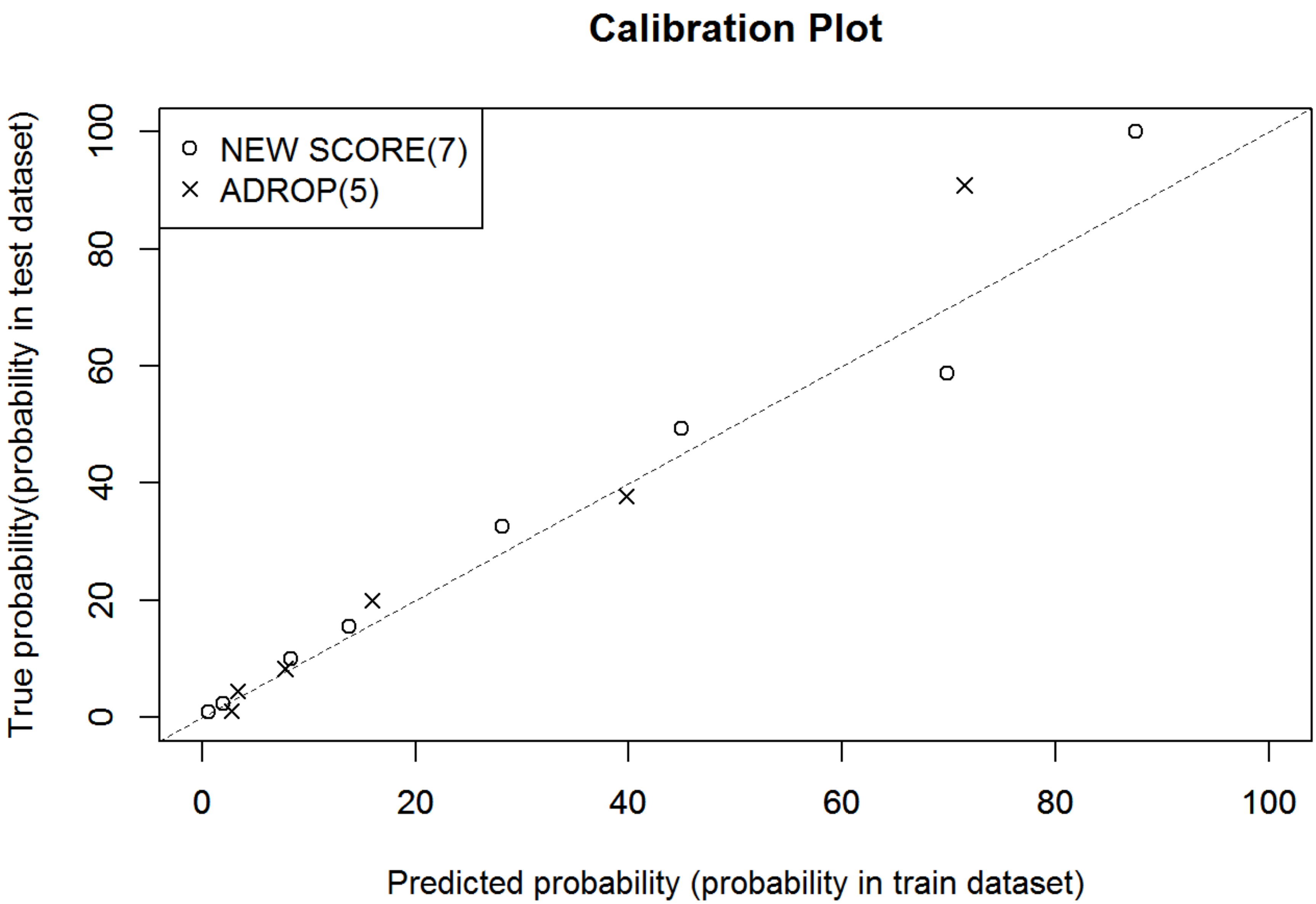
1) “New score” *(0-7)*
2) “A-DROP without dehydration” *(0-4)*
3) “A-DROP” *(0-5)*

Figure.3



1.0
0.8
0.6
0.4
0.2
0.0
Sensitivity
NEW SCORE(7) 0.8017
ADROP without BUN(4) 0.7565
ADROP(5) 0.7372
0.0
0.5
1.0
1 - Specificity

Figure.4



Calibration Plot
NEW SCORE(7)
ADROP(5)
True probability(probability in test dataset)
Predicted probability (probability in train dataset)
0
20
40
60
80
100
0
20
40
60
80
100

Table.1 The summary of the baseline characteristics and an outcome of the patients in the training and test datasets

	Number of patients in training data (%)	Number of patients in test data (%)
Age (mean (sd))	73.07 (11.01)	73.42 (11.06)
Age categorized (%)		
18-64 years	905 (22.8)	348 (21.3)
65-69 years	596 (15.0)	259 (15.9)
70-74 years	699 (17.6)	289 (17.7)
75-79 years	693 (17.5)	252 (15.5)
80-84 years	587 (14.8)	273 (16.7)
85-89 years	378 (9.5)	157 (9.6)
90-94 years	109 (2.8)	52 (3.2)
Sex, female(%)	1106 (27.9)	478 (29.3)
Body mass index (mean (sd))	20.80 (3.79)	20.95 (3.96)
Body mass index categorized (%)		
Severe, moderate thinness: < 17 kg/m^2	524 (13.2)	216 (13.3)
Mild thinness: 17-18.5 kg/m^2	587 (14.8)	248 (15.2)
normal: 18.5-25 kg/m^2	2386 (60.1)	936 (57.4)
Pre-obese: 25-30 kg/m^2	390 (9.8)	182 (11.2)
obese: ≥ 30 kg/m^2	80 (2.0)	48 (2.9)
Arterial oxygen saturation (<90) (%)	1526 (38.5)	604 (37.1)
Systolic blood pressure (<90) (%)	364 (9.2)	112 (6.9)
Blood urea nitrogen (BUN) ≥ 210 mg/L or dehydration	3043 (76.7)	1257 (77.1)
Orientation disturbance (%)	475 (12.0)	174 (10.7)
CRP 200 mg/L or extent of consolidation on chest X-ray ≥2/3 of one lung (%)	952 (24.0)	383 (23.5)
Ambulance use (%)	1045 (26.3)	427 (26.2)
Recent hospitalization (90 days) (%)	1362 (34.3)	519 (31.8)
Undergoing hemodialysis (%)	3230 (81.4)	1293 (79.3)
Undergoing peritoneal dialysis (%)	141 (3.6)	62 (3.8)
Comorbidities		
Diabetes (%)	855 (21.6)	358 (22.0)
Cancer (%)	277 (7.0)	114 (7.0)

Heart disease (%)	991 (25.0)	381 (23.4)
Cerebrovascular disease (%)	358 (9.0)	177 (10.9)
Liver disease (%)	29 (0.7)	10 (0.6)
Activity of daily living		
Feeding (%)	1583 (39.9)	639 (39.2)
Transfer (%)	2274 (57.3)	926 (56.8)
Grooming (%)	1824 (46.0)	742 (45.5)
Toilet use (%)	2058 (51.9)	841 (51.6)
Bathing (%)	2262 (57.0)	921 (56.5)
Mobility on level surface (%)	2310 (58.2)	924 (56.7)
Stairs (%)	2390 (60.2)	967 (59.3)
Dressing (%)	2188 (55.2)	874 (53.6)
Bowel control (%)	1539 (38.8)	660 (40.5)
Bladder control (%)	1531 (38.6)	654 (40.1)
Outcome		
Death (%)	437 (11.0)	194 (11.9)

Table.2 Results of the multivariate analysis of in-hospital mortality in four models

	Model.1 Full model	Model.2 Step wise	Model.3 LASSO	Model.4 Random forest
Male (reference: female)	1.35 (1.04 to 1.76)	1.37	1.25	19.3
Age (reference: 18-64 years)				
65-69 years	2.06 (1.26 to 3.38)	2.14	1.26	83.8
70-74 years	1.61 (1.01 to 2.60)	1.65	dropped	
75-79 years	3.56 (2.32 to 5.58)	3.72	2.24	
80-84 years	3.22 (2.08 to 5.10)	3.39	2.03	
85-89 years	3.41 (2.12 to 5.56)	3.59	2.12	
90-94 years	2.72 (1.33 to 5.38)	2.86	1.58	
Body mass index (reference: normal: 18.5-25 kg/m^2)				
Severe, moderate thinness: <17 kg/m^2	1.97 (1.46 to 2.65)	1.98	1.83	48.6
Mild thinness: 17-18.5 kg/m^2	1.16 (0.84 to 1.58)	1.17	1.09	
Pre-obese: 25-30 kg/m^2	0.72 (0.43 to 1.16)	0.69	0.76	
obese: ≥30 kg/m^2	1.05 (0.33 to 2.71)	1.10	dropped	
Arterial oxygen saturation (<90)	1.88 (1.48 to 2.39)	1.86	1.80	27.1
Systolic blood pressure (<90)	3.15 (2.33 to 4.25)	3.20	2.95	37.0
Blood urea nitrogen (BUN) ≥ 210 mg/L or dehydration	0.90 (0.66 to 1.26)	dropped	dropped	16.0
Disturbance of orientation	2.62 (1.99 to 3.45)	2.62	2.59	42.0
CRP 200 mg/L or extent of consolidation on chest X-ray ≥2/3 of one lung	1.93 (1.51 to 2.47)	1.90	1.81	25.3
Undergoing hemodialysis	0.56 (0.43 to 0.73)	0.58	0.60	22.4
Undergoing peritoneal dialysis	0.61 (0.24 to 1.32)	dropped	0.73	4.3

Ambulance use	0.98 (0.76 to 1.26)	dropped	dropped	21.2
Recent hospitalization (90 days)	1.47 (1.16 to 1.85)	1.45	1.39	23.9
Comorbidities				
Diabetes	0.87 (0.65 to 1.16)	dropped	0.93	17.9
Cancer	1.28 (0.85 to 1.89)	dropped	1.25	14.0
Heart disease	0.91 (0.70 to 1.18)	dropped	0.98	20.6
Cerebrovascular disease	0.59 (0.38 to 0.87)	0.58	0.66	12.9
Liver disease	1.88 (0.53 to 5.57)	dropped	1.54	2.9
Activity of daily living				
Feeding (%)	1.48 (1.00 to 2.20)	1.57	1.41	16.5
Transfer (%)	1.13 (0.61 to 2.09)	dropped	1.02	6.3
Grooming (%)	1.06 (0.65 to 1.75)	dropped	1.001	11.9
Toilet use (%)	1.36 (0.71 to 2.68)	dropped	1.28	7.2
Bathing (%)	0.89 (0.45 to 1.80)	dropped	dropped	5.1
Mobility on level surface (%)	1.09 (0.51 to 2.34)	dropped	dropped	5.4
Stairs (%)	1.04 (0.44 to 2.35)	dropped	dropped	3.5
Dressing (%)	0.75 (0.39 to 1.45)	dropped	dropped	5.6
Bowel control (%)	3.47 (1.35 to 8.74)	2.25	2.00	17.9
Bladder control (%)	0.57 (0.23 to 1.43)	dropped	dropped	13.8

Abbreviation: OR; odds ratio, CI; confidence interval,

“dropped” was not selected as a predictor in each model.

Table.3 C-statistics of all combinations in the training dataset

Without hemodialysis	High CRP or extent of chest X-p	Body mass index <17 kg/m²	ADL dependence	Recent hospitalization	C-statistics in training dataset
					0.7543
		+			0.7665
			+		0.7931
		+	+		0.7977
				+	0.7530
		+		+	0.7625
			+	+	0.7891
		+	+	+	0.7945
	+				0.7664
	+	+			0.7765
	+		+		0.8009
	+	**+**	**+**		**0.8069 ***
	+			+	0.7637
	+	+		+	0.7744
	+		+	+	0.7989
	+	+	+	+	0.8052
+					0.7446
+		+			0.7561
+			+		0.7830

+		+	+		0.7900
+				+	0.7458
+		+		+	0.7592
+			+	+	0.7883
+		+	+	+	0.7916
+	+				0.7513
+	+	+			0.7648
+	+		+		0.7898
+	+	+	+		0.798
+	+			+	0.7562
+	+	+		+	0.7702
+	+		+	+	0.7928
+	+	+	+	+	0.8016

*: highest value of c-statistics

ADL; Activities of daily living, "ADL dependence" means the need for assistance with feeding or bowel control

High CRP or extent of chest X-p; CRP level (over 200 mg/L) or the extent of consolidation on chest radiography (≥2/3 of one lung)

Table.4 Sensitivity and specificity of each score in the test dataset

New score	Total patient number	Number of death (%)	Sensitivity	Specificity
0	**223**	**2 (0.9%)**	**(100 %)**	**(0 %)**
1	**439**	**10 (2.3)**	**99.0**	**15.4**
2	**453**	**45 (9.9)**	**93.8**	**45.3**
3	**284**	**44 (15.5)**	**70.6**	**73.7**
4	**144**	**47 (32.6)**	**47.9**	**90.4**
5	**67**	**33 (49.3)**	**23.7**	**97.1**
6	**17**	**10 (58.8)**	**6.7**	**99.5**
7	**3**	**3 (100.0)**	**1.5**	**100**

Sensitivity and specificity were calculated in test dataset after been grouped into two; one includes the same score or more, and the other includes only less than the score.