

Original Research

A Novel Nomogram for Predicting the Risk of Acute Heart Failure in Intensive Care Unit Patients with COPD

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Running Head: Acute Heart Failure and COPD

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Abbreviations: AHF=acute heart failure; COPD=chronic obstructive pulmonary disease; MIMIC=Medical Information Mart for Intensive Care; LASSO=least absolute shrinkage and selection operator; AUC=area under the curve; ROC=receiver operating characteristic; DCA=decision curve analysis; C-index=Concordance index; RBC=red blood cells; WBC=white blood cells; MCV=mean corpuscular volume; BUN=blood urea nitrogen; INR=international normalized ratio; PT=prothrombin time; PTT=partial thromboplastin time; RDW=red blood cell distribution width; MCH=mean corpuscular hemoglobin; MCHC=mean corpuscular hemoglobin concentration; BE=base excess; ALT=glutamic pyruvic transaminase; AST=glutamic oxaloacetic transaminase; ALP=alkaline phosphatase; TBIL=total bilirubin; BMI=body mass index; pco₂=partial pressure of carbon dioxide

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Abstract

Background: The objective of this study was to construct a prediction model to assess the onset of acute heart failure (AHF) in patients with chronic obstructive pulmonary disease (COPD) without history of heart failure and to evaluate the predictive value of the nomogram.

Methods: This study involved 3,730 patients with COPD and no history of heart failure.

Clinical and laboratory data were collected from the Medical Information Mart for Intensive Care IV (MIMIC-IV) database. The patients were divided into a training set (2,611 cases) and a validation set (1,119 cases) in a 7:3 ratio. Least absolute shrinkage and selection operator (LASSO) regression was used to identify potential risk factors for AHF in patients with COPD. These factors were then subjected to multivariate logistic regression analysis to develop a prediction model for the risk of AHF. The model's differentiation, consistency, and clinical applicability were evaluated using receiver operating characteristic (ROC) analysis, a calibration curve, and decision curve analysis (DCA), respectively.

Results: LASSO regression identified 10 potential predictors. The concordance index was 0.820. The areas under the curves for the training and validation sets were 0.8195 and 0.8035, respectively. The calibration curve demonstrated strong concordance between the nomogram's predictions and the actual outcomes. DCA confirmed the clinical applicability of the nomogram.

Conclusion: Our nomogram is a reliable and convenient tool for predicting acute heart failure in patients with chronic obstructive pulmonary disease.

Pre-proof

Introduction

COPD is a chronic respiratory disorder manifesting as progressive and partially reversible airflow restriction, whose exact cause is not yet fully understood, but it is believed to be related to abnormal inflammatory reactions in the lungs [1, 2]. The incidence of COPD gradually increases with the aging of the population, and about 10% of the total population suffers from it [1, 3]. Now it is the third leading cause of death in the United States [4]. COPD is largely believed to be caused by tobacco, but about half of all COPD cases worldwide are due to non-tobacco-related risk factors, such as air pollution, occupational exposures, poorly controlled asthma, infectious diseases and so on [5].

Comorbidities are common in COPD and seriously reduce the quality of life of patients, with the role of heart failure becoming increasingly prominent [3, 6]. COPD and heart failure share overlapping pathophysiological processes to some extent [7-9]. Therefore, it is reasonable for a certain proportion of COPD patients to have associated heart failure. The incidence of underlying heart disease is greater in patients with moderate or severe airflow limitation [8, 10]. However, the relationship between COPD and cardiovascular diseases is not thoroughly figured out. Evidence shows that COPD is associated with low grade inflammation, which is also found in AHF patients [11-13].

Nomograms are widely used in oncology and pharmacy to determine the prognosis and evaluate the likelihood of specific events [14]. However, predictive models for assessing the incidence of AHF in patients with COPD remain limited. This study utilized data from the “Medical Information Mart for Intensive Care” (MIMIC) database to develop and validate a nomogram for predicting the onset of AHF in patients with COPD. Although this nomogram can help

identify a subset of patients with COPD at risk of respiratory failure, for which heart failure may be a potential contributor, its utility is limited in patients with respiratory failure of unknown etiology. This limitation is also observed with other markers, such as brain natriuretic peptide.

Methods

Database

The data for this study were obtained from the MIMIC-IV v2.2 database, which is a publicly available and free database in the field of critical care medicine. The data were sourced from the intensive care unit of Beth Israel Deaconess Medical Center in Boston, Massachusetts, USA from 2008 to 2019 [15-17]. PostgreSQL v16 was used to search and extract data from it (<http://www.postgresql.org/>).

Study population

It has been demonstrated that patients with COPD and a history of heart failure are at an elevated risk of experiencing another acute cardiovascular event due to an acute exacerbation of COPD from various causes [18]. Accordingly, the present study included only COPD patients without a history of heart failure in order to avoid the potential confounding influence of a previous history of heart failure on new-onset AHF.

The inclusion criteria were as follows:

1. Patients with previous history of COPD but no history of heart failure.
2. Patients aged older than 18 years.

3. Patients admitted to the ICU for the first time.

Patient diagnoses were captured using ICD-9 and ICD-10 codes. We included patients with acute diastolic heart failure (42831, I5031), patients with acute systolic heart failure (42821, I5021), patients with acute combined systolic and diastolic heart failure (42841, I5041) and patients with acute right heart failure (I50811).

Data collection and measurements

Demographic data (e.g., age, gender, race and marital status), vital signs (e.g., heart rate, and mean blood pressure), laboratory results (e.g., routine blood tests, chemistry and coagulation) and ventilation data were extracted based on MIMIC-IV data availability and previous literature reviews on risk factors for AHF. The demographic data were obtained from the registration record at the time of admission to the ICU. Vital signs and ventilation status were obtained from the initial record at the time of admission to the ICU. Laboratory results were extracted within 24 hours of admission to the ICU. In the event of multiple measurements of the same variable within 24 hours, only the initial result was extracted.

Statistical analysis

Statistical analysis was achieved by using R software (Version 4.3.1; R Foundation for Statistical Computing, Vienna, Austria; <https://www.r-project.org>). Continuous data were expressed as mean \pm standard deviation (SD), as median or as quartiles [M (P25, P75)]. Categorical data were expressed as number of cases or percentage (%). Missing data were imputed using the Multivariate Imputation by Chained Equations (MICE) package, which

employs a chained equations approach [19]. To avoid making the nomogram too complex, the lambda value was set to '1se'. The bootstrap resampling was performed 1000 times [20]. DCA was used to identify the clinical benefit of the model [21]. The ROC curves and area under the ROC curve (AUC) for each subject were plotted [22]. All statistical tests were conducted using two-sided tests, and differences were considered statistically significant at a level of $P < 0.05$.

Results

Clinical characteristics

Supplementary Figure 1 is a flowchart showing the cohort selection process. Table 1 summarizes the data of the enrolled variables. Of the 3730 patients with COPD, 1002 were admitted to the ICU for an AHF. [Table 1 near here] Table 1 Data of variables enrolled in this study

Variable selection

Any data with more than 5% missing values was deleted, while data with less than 5% missing values was replaced via chained equations. Of 90 variables extracted, 55 variables were examined (Supplementary Figure 2). Supplementary Figure 3 shows ROC curves of all screened variables. Supplementary Figure 4 is a heatmap involving all screened variables. Supplementary Figure 5 illustrates AUC values of all variables. Twentyfold cross-validated LASSO regression identified ten variables: age, body mass index (BMI), urine output, partial pressure of carbon dioxide (pco₂), bicarbonate, partial thromboplastin time (PTT), total bilirubin (TBIL), urea, chloride and ventilation status. Figure 1 illustrates the variable selection

process. These ten variables were included in the multivariate Logistic regression model for predicting the occurrence of AHF, and their odd ratios and 95% confidence intervals (CIs) were 1.92(1.63~2.25), 1.34(1.19~1.51), 1.40(1.25~1.56), 0.72(0.62~0.85), 2.27 (1.95~2.65), 1.46 (1.30~1.65), 0.75(0.68~0.82), 1.93(1.73~2.15), 0.71(0.63~0.80) and 0.18-1.65 (0.02-1.11~0.67-2.43), respectively. The values of troponin-T and N-terminal pro-b-type natriuretic peptide were missing in more than 50% and 70% of patients, respectively. Due to limitations in the data presentation, it was unclear whether certain tests (e.g., troponin measurements) had been performed but not recorded in the database or whether the tests had not been performed at all. Consequently, these variables were excluded from the study. These variables are well established as critical indicators of heart failure, their exclusion inevitably reduced the comprehensiveness of the nomogram. However, we determined that their exclusion was necessary to ensure the stability and completeness of the model.

Construction of a nomogram

The results of the logistic regression analysis were used to construct a nomogram for predicting the occurrence of AHF in patients with COPD (Figure 2). To calculate the score, a vertical line was drawn from each variable to the "Points" line. The points for all variables were then summed to determine the total score. Finally, a vertical line was drawn downward from the "Total Points" line to determine the probability of AHF in patients with COPD.

Online platform

Based on the nomogram, we constructed an online platform

(<https://wuziyang.shinyapps.io/DynNomapp/>).

The user may select the value of each variable with the mouse and obtain the predicted probability by clicking the "Predict" button.

Assessment and validation

The C-index for the prediction of AHF was 0.820, indicating that the nomogram demonstrated robust discriminatory capacity. The calibration curve showed strong concordance with the actual incidence (Figure 3). The ROC curve and AUC were plotted to evaluate the model's predictive performance. The AUC was 0.8195 in the training set and 0.8035 in the validation set (Figure 4), conforming that the nomogram had good predictive ability. Figure 5 demonstrates the clinical availability and net benefit of the nomogram, indicating a net gain in AHF risk in the validation cohort.

Discussion

This population-based study retrospectively investigated 3730 patients admitted to the ICU with COPD. A nomogram model was developed and validated to gauge the risk of AHF. The nomogram contained ten variables: age, BMI, urine output, pCO₂, bicarbonate, PTT, TBIL, urea, chloride and ventilation status. It demonstrated good clinical utility. The ROC analysis of the training cohort had an AUC of 0.8195 and that of the test cohort was 0.8035, suggesting that our model is predictive. When using the nomogram to estimate the probability of developing AHF, users can draw a vertical line from the value of each variable to the "Points"

line to obtain a score for that variable. The scores for all variables are then summed to calculate the total score. Finally, a vertical line is drawn downward from the total score to determine the specific probability of AHF.

Researchers in respirology and cardiology have examined the relationship between COPD and heart failure. However, no consensus has yet been reached. Many papers have hypothesized about the mechanisms by which heart failure and COPD interact [23, 24].

A common risk factor for COPD and heart failure is age [25]. The prevalence of COPD and heart failure increases with age. Due to the prolongation of life expectancy worldwide, the proportion of patients is gradually increasing [1, 26, 27]. Our model shows that increasing age leads to an increased probability of AHF occurrence. This is consistent with existing conclusions. In our model, a high BMI is indicative of an elevated risk of developing AHF. Prior research has demonstrated a positive correlation between obesity and the incidence of cardiovascular disease [28]. Nevertheless, it is still debatable whether BMI can be considered an independent indicator of obesity when other factors such as waist circumference are present [29]. Our nomogram indicates that higher urine output is associated with an increased risk of AHF, which may appear counterintuitive. A possible explanation for this finding is the excessive use of diuretics [30]. In clinical practice, ventilation is a common and widely utilized treatment for patients with COPD and AHF. Low $p\text{CO}_2$ is an important manifestation of hyperventilation and is closely associated with poor prognosis in AHF patients [31, 32]. Our nomogram shows a decrease in $p\text{CO}_2$ after AHF in COPD patients, which suggests that clinicians should be more cautious when deciding on ventilation therapy. In patients with AHF, the use of diuretics and the resulting contraction alkalosis due to dehydration can elevate blood

bicarbonate levels, a result that aligns with the predictions of our model [33]. Some big data studies indicate that PTT is a risk factor for heart failure [34-36]. Further research is needed on the pathophysiological principles involved. Liver congestion and hepatic insufficiency resulting due to circulatory disturbances are commonly observed in patients with heart failure [37, 38]. However, our nomogram did not include other liver-related markers, such as alkaline phosphatase, glutamic oxaloacetic transaminase, or glutamic pyruvic transaminase. As a result, it cannot be concluded that total bilirubin independently reflects liver function. As is shown in our nomogram, worsening or lack of improvement in blood urea nitrogen (BUN) during hospitalization is a poor predictor for AHF patients [39]. The nomogram also reveals that patients with COPD who develop AHF tend to have low blood chloride concentrations. This finding may be linked to the use of diuretics and the development of alkalosis. Previous studies have proposed that a low blood chloride concentration is a predictor of a poor prognosis in heart failure [40-42]. These findings are consistent with the result of our study, in which blood chloride was included as a variable in the nomogram. Currently, research on the relationship between different ventilation patterns and heart failure has not been conducted. Our model lists ventilation patterns as influencing factors for heart failure, and further in-depth research can be conducted in the future.

Clinicians need to evaluate patients with COPD before deciding on treatment plans. The identification of predictive factors and risk assessment is crucial to prevent the occurrence of AHF. A nomogram is a total score based on the values of multiple predictor variables for an individual [43]. The variables included in our model are commonly encountered and available in clinical work in ICUs. Before using the nomogram, clinicians must determine whether the

patient falls within its scope of applicability. As noted earlier, the nomogram is suitable for patients with respiratory failure in which AHF may be a potential contributor. However, in patients with COPD who have respiratory failure of unknown etiology, the performance of the nomogram is suboptimal.

Our study has some limitations. Firstly, all of our data came from the MIMIC-IV database. Incomplete records and possible data errors may have reduced the accuracy of our model. Secondly, this was a single-center retrospective study. Only internal validation was performed, so external validation is needed to confirm the reliability of the results. Thirdly, blood lipids were not included in the study due to the lack of corresponding records in the MIMIC-IV database. Blood lipids are important risk factors for cardiovascular diseases [44], so further research on them is necessary. Fourthly, the types and severity of COPD were not considered in this study, which did not determine the risk of developing AHF for each severity level of COPD. In addition, all types of AHF were lumped together. Fifthly, the application of this nomogram to a population of COPD patients with unexplained respiratory failure is not recommended. Sixthly, including diuretic use in the model would be optimal. However, due to data limitations, we were only able to include urine output. Seventhly, while equity analysis is crucial to any type of clinical model, it is not feasible to conduct such an analysis in our study [45, 46]. Finally, our nomogram may predict the possibility of AHF in patients with COPD, but cannot answer whether intervention was prompt.

Conclusion

Using data from the MIMIC-IV database, we developed a nomogram to predict the risk of AHF

in patients with COPD. The model demonstrated good predictive performance. This nomogram can assist in identifying patients with COPD at risk of AHF and support clinicians in making informed clinical decisions.

Pre-proof

Declarations

Acknowledgements

We would like to thank all MIMIC project team members.

Ethics approval and consent to participate

This study is a retrospective analysis of data stored in a public database. All information is available and free for the public, so the agreement of the medical ethics committee board and the need for informed consent were not necessary.

Consent for publication

Not applicable.

Availability of data and materials

The datasets used/or analyzed during the current study are available from the corresponding author on reasonable request.

Conflicts of Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Author contributions

Ziyang Wu conceived, designed the study and drafted the manuscript. Sutong Zhan revised the

manuscript. Chengchun Tang and Dong Wang revised the manuscript and approved the final version to be published. All authors read and approved the final manuscript.

Preprint

There is a preprint with the same title in Research Square.

Link: <https://www.researchsquare.com/article/rs-3724657/v1>.

Pre-proof

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Pre-proof

Table 1 Data of variables enrolled in this study

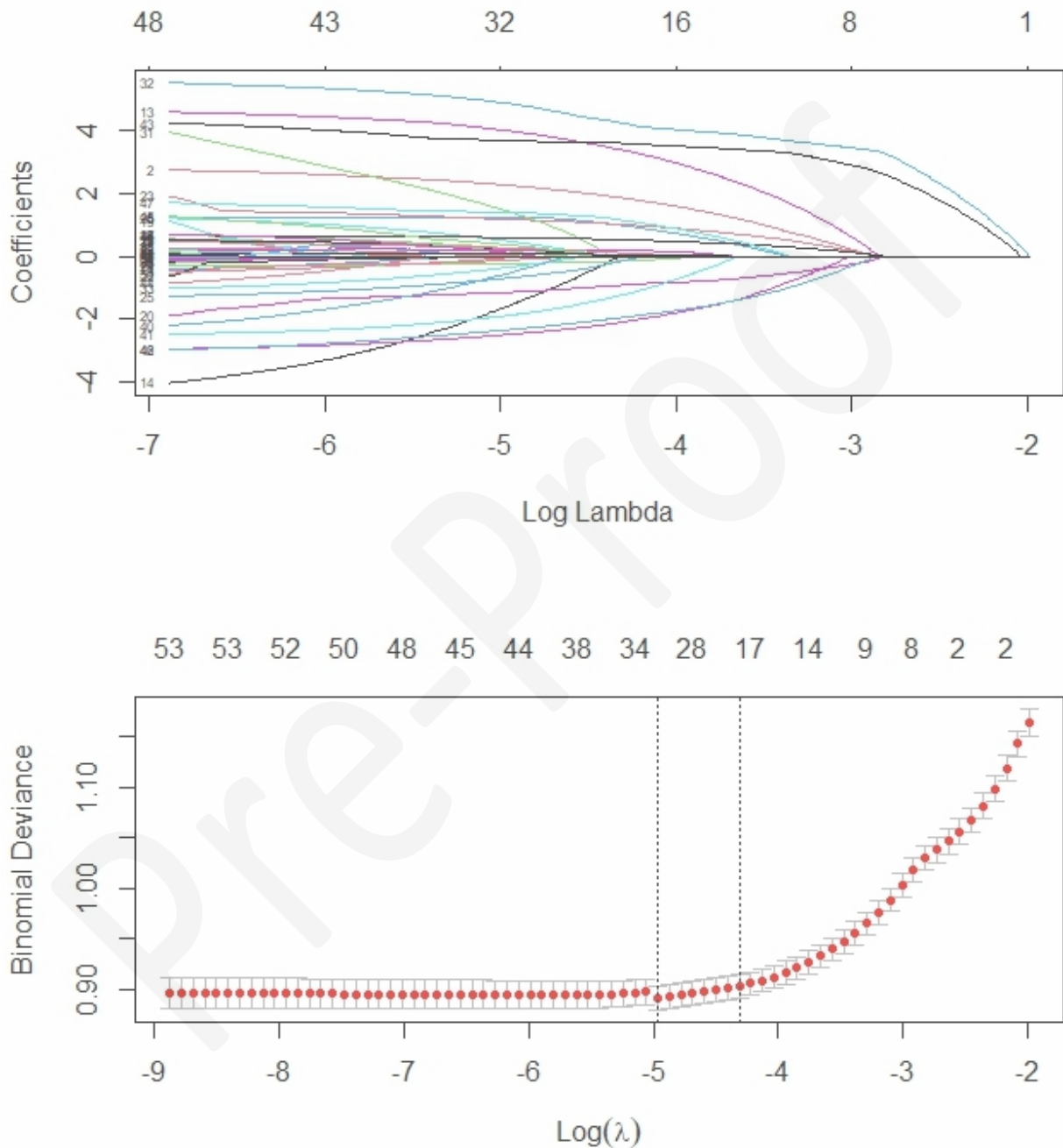
Variables	Total (n = 3730)	N ₀ (2728)	N ₁ (1002)	p
gender, n (%)				0.082
female	1783 (48)	1280 (47)	503 (50)	
male	1947 (52)	1448 (53)	499 (50)	
age, Median (Q1,Q3)	72.07 (64.09, 80.15)	71.04 (63.01, 78.89)	75.03 (67.11, 82.71)	< 0.001
height, Median (Q1,Q3)	170 (160, 180)	170.5 (160, 180)	170 (160, 180)	0.919
weight, Median (Q1,Q3)	79 (64.9, 96.6)	77.6 (64, 93.73)	83.35 (67.74, 102.9)	< 0.001
BMI, Median (Q1,Q3)	27.1 (22.23, 33.42)	26.56 (21.93, 32.6)	28.93 (23.2, 35.64)	< 0.001
marital_status, n (%)				0.004
unmarried	1003 (27)	761 (28)	242 (24)	
married	1529 (41)	1097 (40)	432 (43)	
divorced	464 (12)	358 (13)	106 (11)	
widowed	676 (18)	467 (17)	209 (21)	
others	58 (2)	45 (2)	13 (1)	
race, n (%)				0.717
white people	2565 (69)	1881 (69)	684 (68)	
people of other races	1165 (31)	847 (31)	318 (32)	
heartrate, Median (Q1,Q3)	101 (83, 116)	101 (81, 115)	102 (89, 120)	0.072
meanbp, Median (Q1,Q3)	60 (53, 87.5)	60 (54, 88.5)	58.5 (52, 85)	< 0.001
resprate, Median (Q1,Q3)	28 (25, 33)	28 (24, 33)	29 (26, 33)	< 0.001
temp, Median (Q1,Q3)	36.94 (36.33, 37.28)	37 (36.33, 37.33)	36.89 (36.33, 37.28)	0.004
spo2, Median (Q1,Q3)	96.23 (94.56, 97.55)	96.26 (94.6, 97.62)	96.08 (94.46, 97.38)	0.041
urineoutput, Median (Q1,Q3)	1375 (825, 2150)	1320 (805, 2010)	1585 (887.75, 2625)	< 0.001
WBC, Median (Q1,Q3)	14.3 (10.5, 19.5)	14.1 (10.4, 19.3)	14.7 (10.9, 20.1)	0.011
RBC, Median (Q1,Q3)	3.86 (3.36, 4.36)	3.86 (3.36, 4.35)	3.84 (3.34, 4.38)	0.794
hemoglobin, Median (Q1,Q3)	11.3 (9.9, 12.8)	11.5 (10, 12.9)	11 (9.5, 12.5)	< 0.001
platelet, Median (Q1,Q3)	254 (190, 344)	253 (189, 341)	256 (193, 348)	0.326
hematocrit, Median (Q1,Q3)	35.8 (31.4, 39.9)	36 (31.6, 39.92)	35.3 (30.9, 39.88)	0.121
MCH, Median (Q1,Q3)	30.3 (28.5, 31.8)	30.4 (28.7, 31.9)	29.9 (27.8, 31.7)	< 0.001
MCHC, Median (Q1,Q3)	32.7 (31.6, 33.8)	32.9 (31.8, 33.9)	32.3 (31.1, 33.3)	< 0.001
MCV, Median (Q1,Q3)	95 (91, 100)	95 (91, 99)	96 (91, 101)	0.041
RDW_SD, Median (Q1,Q3)	54.1 (49.1, 61.1)	52.9 (48.2, 59.5)	57.25 (52.1, 64.3)	< 0.001
RDW, Median (Q1,Q3)	15.9 (14.5, 18.2)	15.6 (14.2, 17.7)	17.1 (15.4, 19.1)	< 0.001
po2, Median (Q1,Q3)	159.5 (82, 285.75)	168 (85, 304.25)	141 (76, 224)	< 0.001
pco2, Median (Q1,Q3)	54 (45, 69)	53 (44, 68)	57 (47.25, 73)	< 0.001
pH, Median (Q1,Q3)	7.42 (7.37, 7.47)	7.42 (7.36, 7.47)	7.43 (7.39, 7.49)	< 0.001
lactate, Median (Q1,Q3)	2.4 (1.6, 4.3)	2.4 (1.6, 4.5)	2.4 (1.6, 3.8)	0.292
Na, Median (Q1,Q3)	143 (140, 146)	143 (140, 146)	143 (140, 146)	0.754

K, Median (Q1,Q3)	4.9 (4.5, 5.5)	4.8 (4.4, 5.4)	5.1 (4.7, 5.7)	< 0.001
Ca, Median (Q1,Q3)	9.1 (8.7, 9.6)	9.1 (8.6, 9.5)	9.3 (8.9, 9.7)	< 0.001
glucose, Median (Q1,Q3)	183 (144, 248.75)	174 (137, 228)	215 (166, 299)	< 0.001
bicarbonate, Median (Q1,Q3)	29 (26, 33)	28 (26, 32)	32 (29, 37)	< 0.001
totalco2, Median (Q1,Q3)	31 (26, 38)	30 (26, 37)	33 (28, 40)	< 0.001
BE, Median (Q1,Q3)	3 (0, 9)	3 (0, 8)	5 (1, 10)	< 0.001
PT, Median (Q1,Q3)	15.2 (12.8, 23.2)	14.7 (12.5, 20.7)	17.2 (13.6, 31.55)	< 0.001
PTT, Median (Q1,Q3)	36.7 (30.1, 84.1)	35 (29.6, 71.82)	44.75 (31.9, 123.57)	< 0.001
INR, Median (Q1,Q3)	1.4 (1.2, 2.1)	1.4 (1.2, 1.9)	1.6 (1.3, 2.9)	< 0.001
ALT, Median (Q1,Q3)	41 (18, 195.75)	45.5 (18, 217)	34 (18, 123.75)	< 0.001
AST, Median (Q1,Q3)	54 (24, 219)	60.5 (24, 244.25)	43 (24, 162.75)	0.003
AST/ALT, Median (Q1,Q3)	1.33 (0.89, 1.97)	1.33 (0.87, 2)	1.35 (0.95, 1.89)	0.429
ALP, Median (Q1,Q3)	119 (78, 242.75)	122.5 (77, 272.25)	111.5 (80, 188)	0.004
TBIL, Median (Q1,Q3)	0.9 (0.5, 4.5)	0.9 (0.5, 6.1)	0.8 (0.4, 1.7)	< 0.001
urea, Median (Q1,Q3)	31 (21, 53)	27 (18, 44)	48 (31, 73)	< 0.001
creatinine, Median (Q1,Q3)	1.2 (0.9, 2.1)	1.1 (0.8, 1.8)	1.7 (1.2, 2.8)	< 0.001
P, Median (Q1,Q3)	4.5 (3.9, 5.5)	4.3 (3.7, 5.2)	5 (4.4, 6)	< 0.001
Cl, Median (Q1,Q3)	106 (102, 109)	106 (103, 110)	104 (100, 108)	< 0.001
AG, Median (Q1,Q3)	18 (15, 21)	17 (15, 20)	19 (16, 22)	< 0.001
o2_flow, Median (Q1,Q3)	2 (2, 4)	2 (2, 4)	2 (2, 4)	< 0.001
ventilation_status, n (%)				< 0.001
non-ventilation	501 (13)	442 (16)	59 (6)	
high-flow nasal cannula oxygen	80 (2)	52 (2)	28 (3)	
invasive vent	1041 (28)	776 (28)	265 (26)	
noninvasive vent	222 (6)	108 (4)	114 (11)	
supplemental oxygen	1849 (50)	1318 (48)	531 (53)	
tracheostomy	37 (1)	32 (1)	5 (0)	
minute_volume, Median (Q1,Q3)	0 (0, 7)	0 (0, 7.1)	0 (0, 6.9)	0.79
tidal_volume, Median (Q1,Q3)	0 (0, 408)	0 (0, 410.5)	0 (0, 401)	0.962
plateau_pressure, Median (Q1,Q3)	0 (0, 14)	0 (0, 14)	0 (0, 16)	0.012
peep, Median (Q1,Q3)	0 (0, 5)	0 (0, 5)	0 (0, 5)	0.076
fio2, Median (Q1,Q3)	35 (21, 60)	35 (21, 60)	40 (21, 60)	0.031
flow_rate, Median (Q1,Q3)	0 (0, 0)	0 (0, 0)	0 (0, 0)	0.882

BMI, body mass index; meanbp, mean blood pressure; resprate, respiratory rate; temp, temperature; WBC, white blood cells; RBC, red blood cells; MCH, mean corpuscular hemoglobin; MCHC, mean corpuscular hemoglobin concentration; MCV, mean corpuscular volume; RDW-SD, red blood cell distribution width-standard deviation; RDW, red blood cell distribution width; BE, base excess; PT, prothrombin time; PTT,

partial thromboplastin time; INR, international normalized ratio; ALT, glutamic pyruvic transaminase; AST, glutamic oxaloacetic transaminase; ALP, alkaline phosphatase; TBIL, total bilirubin; AG, anion gap.

Figure 1 Variable selection process

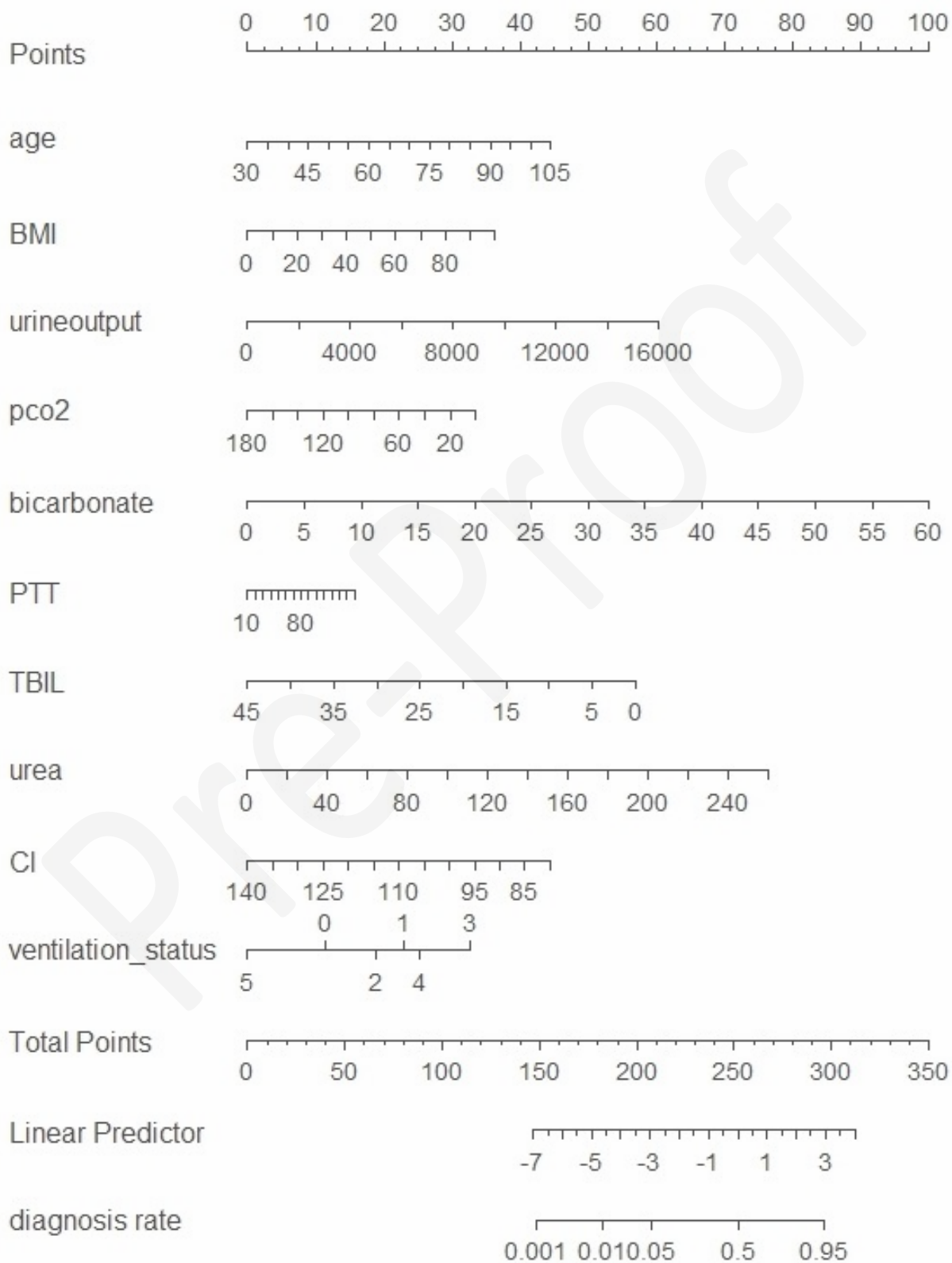


Footnote to Figure 1: The upper horizontal axis indicates the number of variables with non-zero

coefficients at each point in the model. The lower horizontal axis represents the logarithmic value of the penalty coefficient. The dashed line denotes the number of variables corresponding to the model's optimal performance.

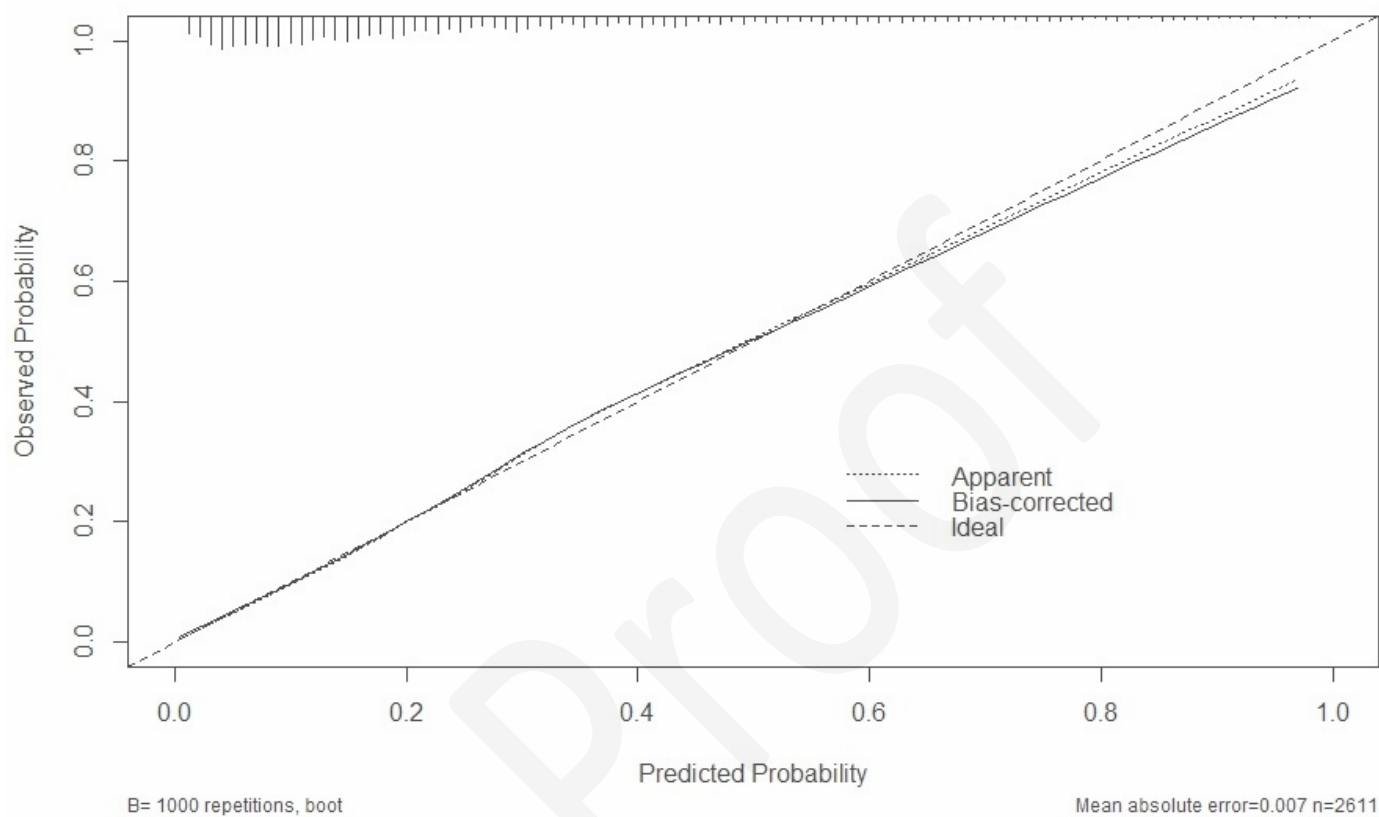
Pre-proof

Figure 2 Nomogram for predicting the occurrence of AHF in COPD patients



Footnote to Figure 2: BMI, body mass index (kg/m^2); pco₂, partial pressure of carbon dioxide (mmHg); PTT, partial thromboplastin time (second); TBIL, total bilirubin (mg/dL); urea, blood urea nitrogen (mg/dL); Cl, chloride (mEq/L); age (year); urineoutput (mL); bicarbonate (mEq/L); ventilation_status, 0: non-ventilation, 1: high-flow nasal cannula oxygen, 2: invasive vent, 3: noninvasive vent, 4: supplemental oxygen, 5: tracheostomy

Figure 3 Calibration curve



Footnote to Figure 3: The x-axis represents the probability of AHF predicted by the model, and the y-axis shows the actual diagnosed risk of AHF. The diagonal dashed line indicates the model's ideal prediction. The close alignment of the curves with the diagonal line reflects the model's robust predictive performance.

Figure 4 The ROC curves of the training set and the validation set

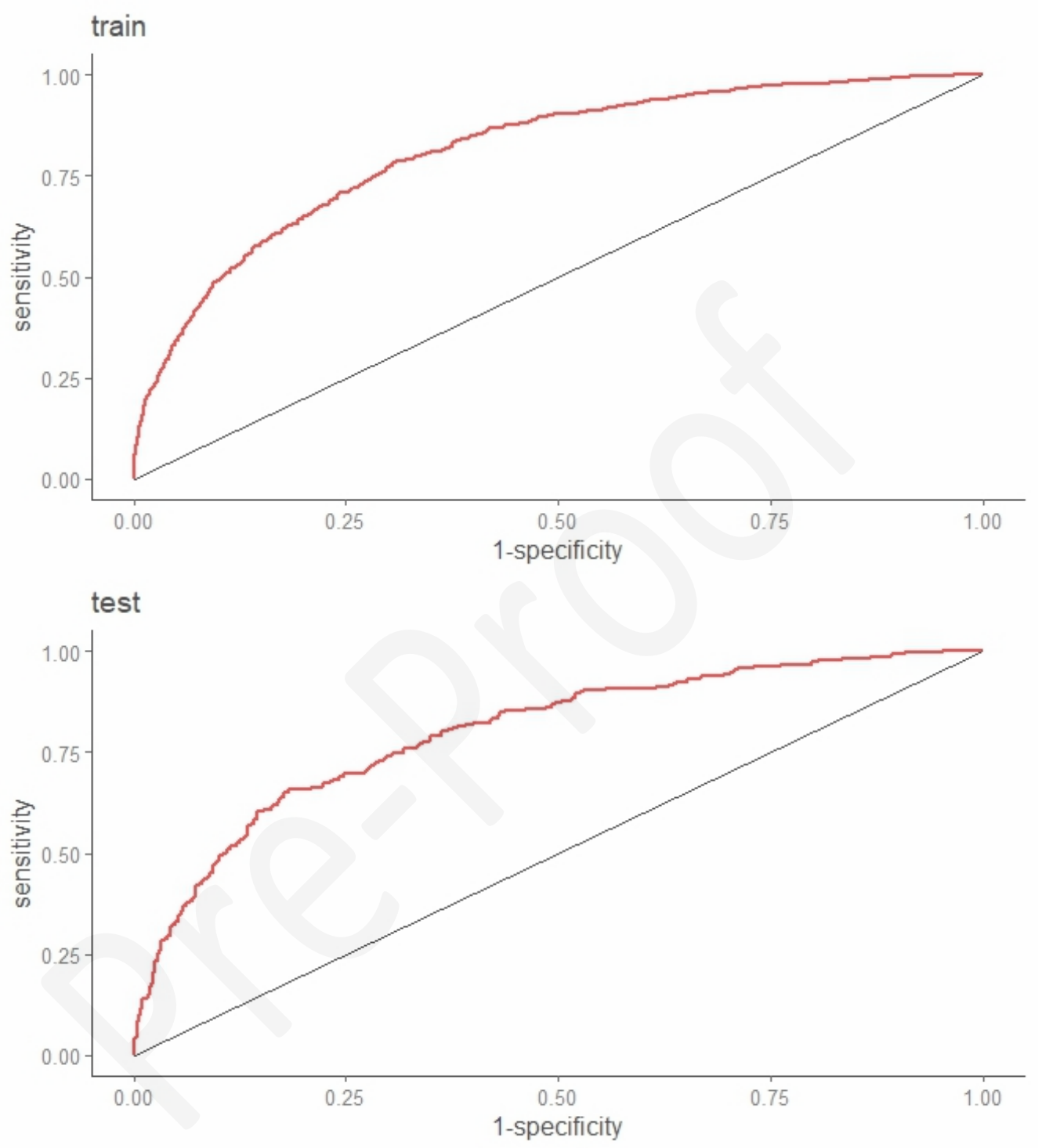
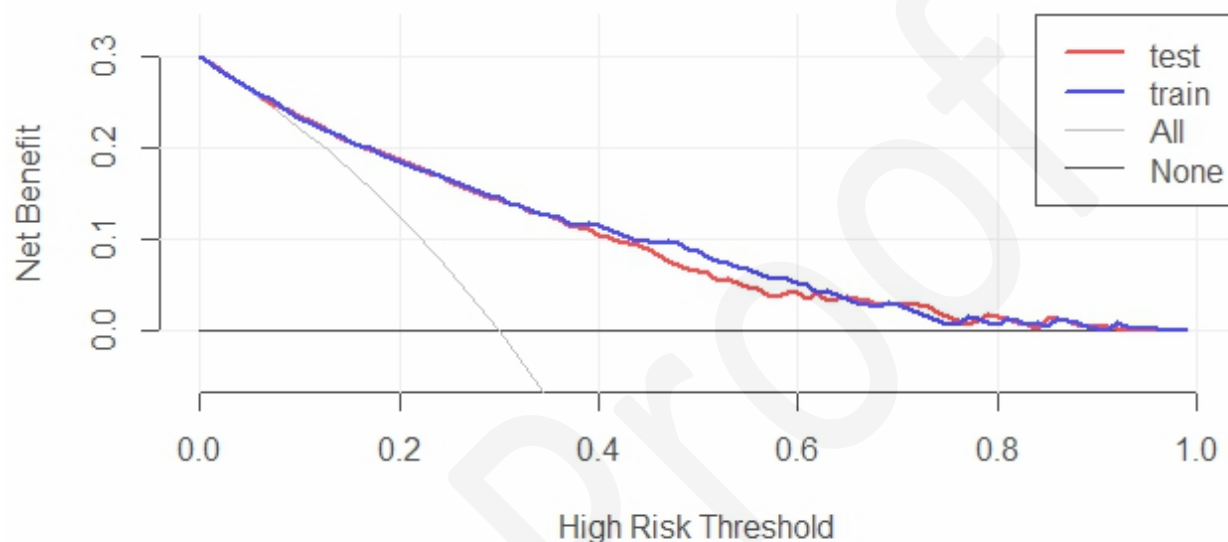


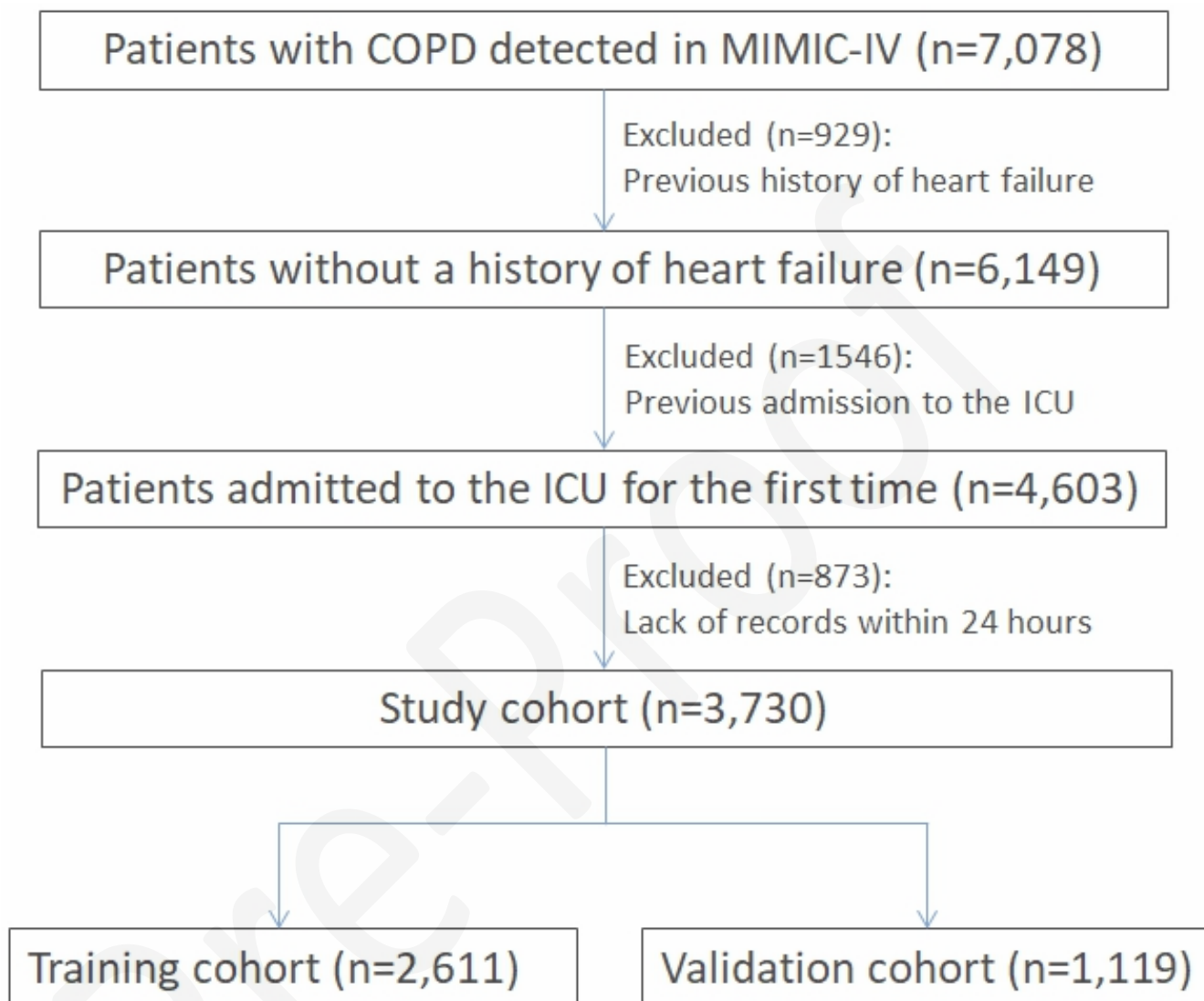
Figure 5 Decision curve analysis



Footnote to Figure 5: The x-axis represents the threshold probability, and the y-axis represents the net benefit. The gray curve assumes that all patients with COPD will develop acute heart failure, while the black straight line assumes that no COPD patients will develop acute heart failure.

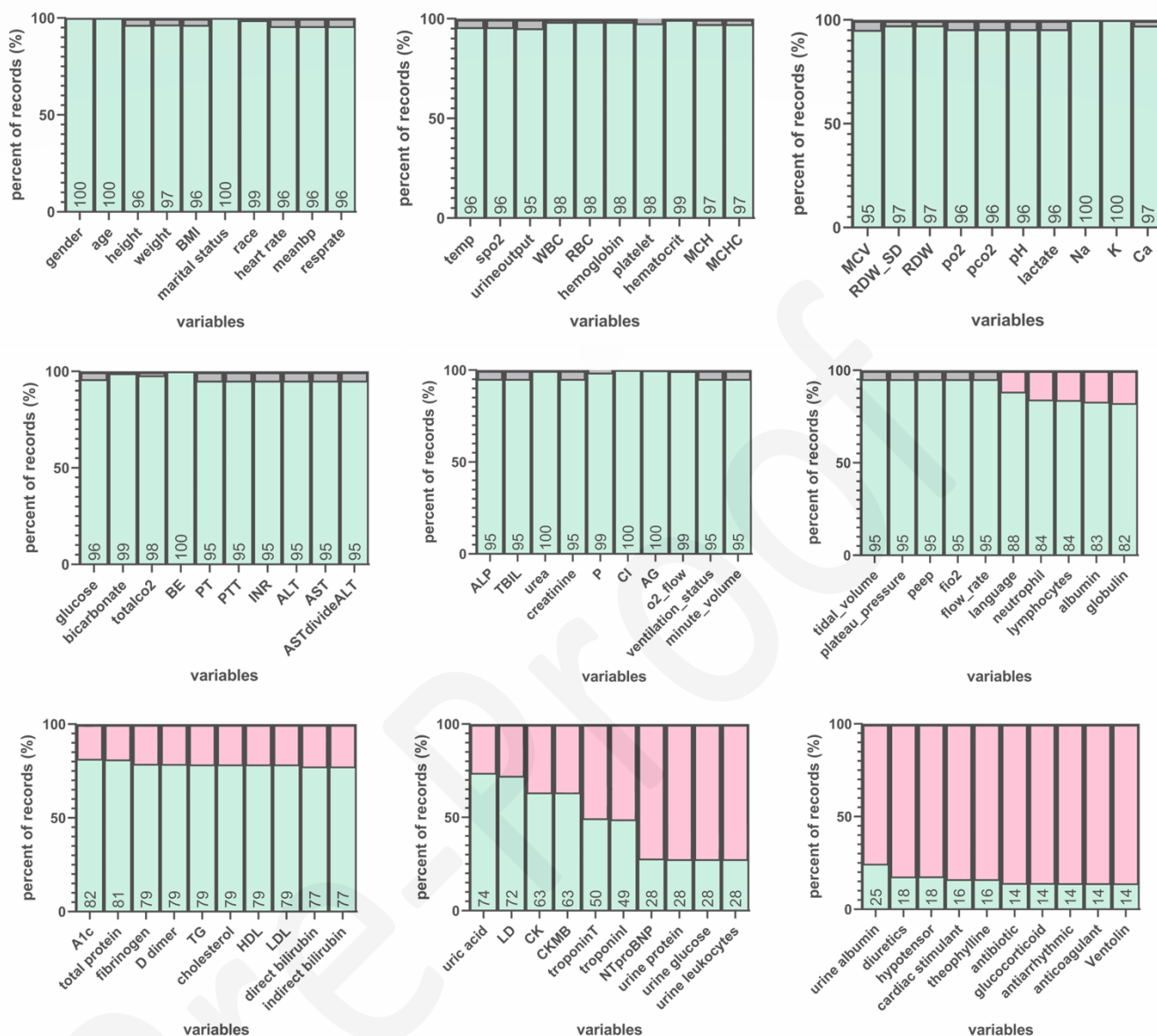
Online Supplement

Supplementary Figure 1 Flowchart showing the cohort selection process



Footnote to Supplementary Figure 1: COPD, chronic obstructive pulmonary disease; MIMIC, Medical Information Mart for Intensive Care; ICU, intensive care unit

Supplementary Figure 2 Proportion of records for all variables

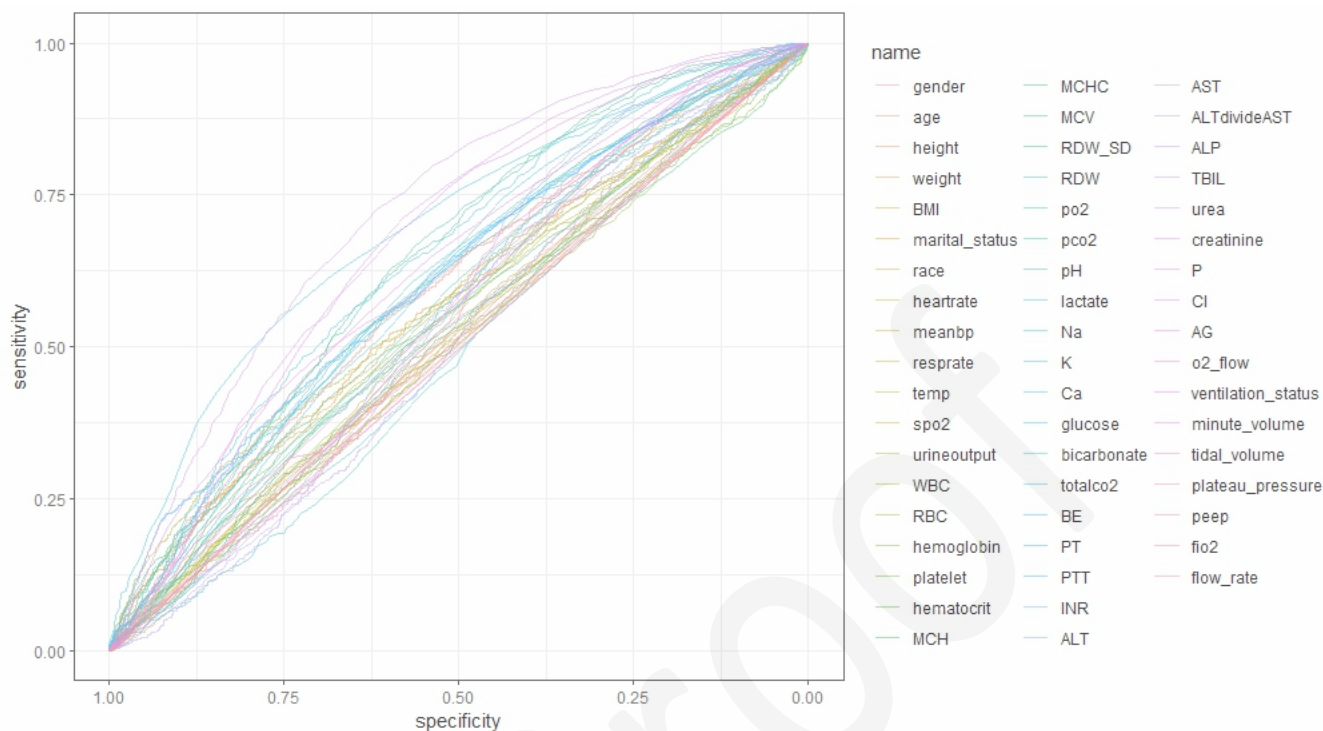


Footnote to Supplementary Figure 2: The green section indicates the percentage of records available in the database for each variable. The gray section represents missing values comprising < 5% of the total, which were imputed. The pink section indicates missing values exceeding 5%, leading to the exclusion of these variables from the analysis.

BMI, body mass index; meanbp, mean blood pressure; resprate, respiratory rate; temp, temperature; spo2, oxygen saturation of blood; WBC, white blood cells; RBC, red blood cells; MCH, mean corpuscular hemoglobin; MCHC, mean corpuscular hemoglobin concentration;

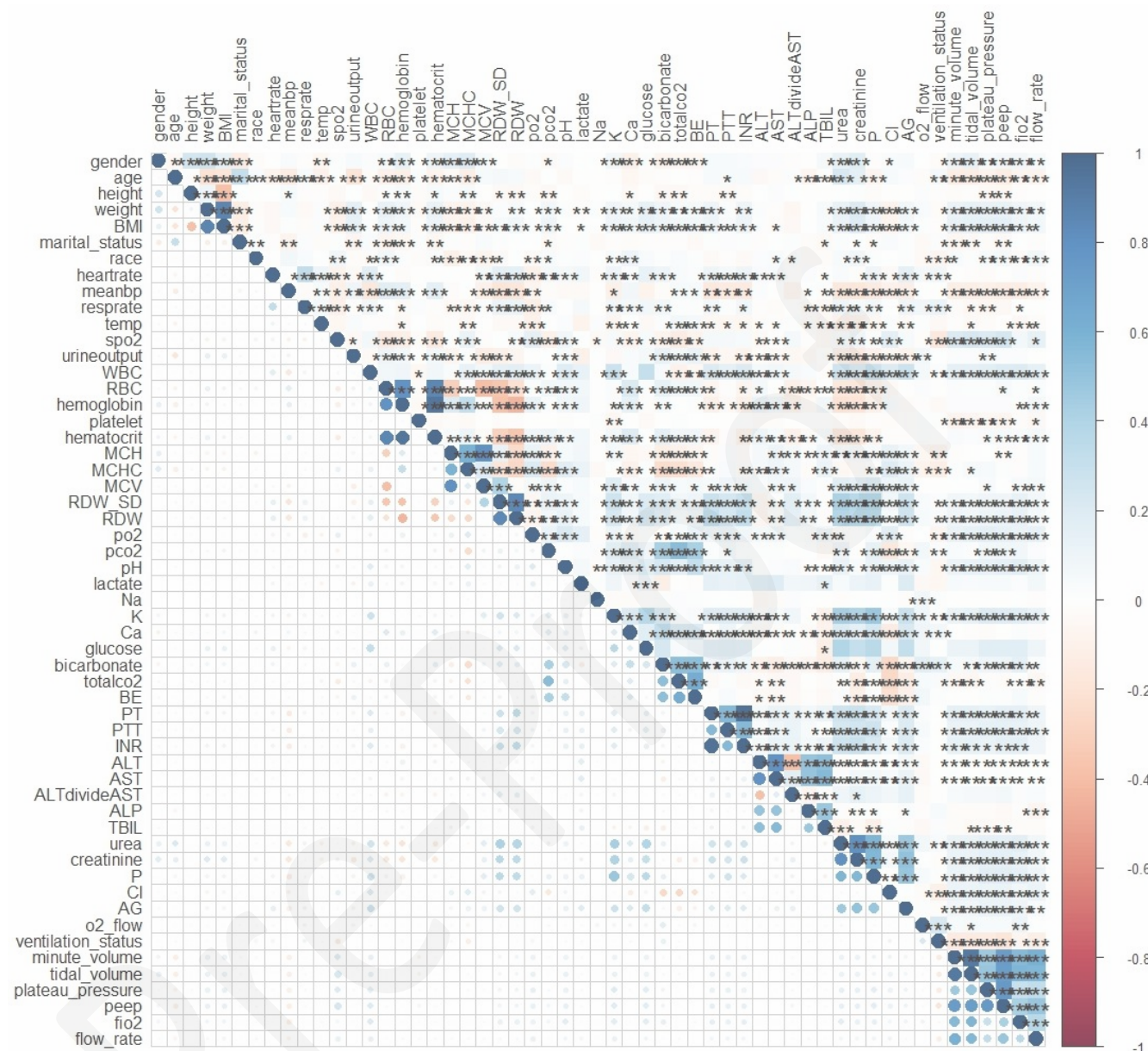
MCV, mean corpuscular volume; RDW, red blood cell distribution width; RDW-SD, red blood cell distribution width-standard deviation; po₂, partial pressure of oxygen; pco₂, partial pressure of carbon dioxide; pH, potential of hydrogen; Na, sodium; K, potassium; Ca, calcium; totalco₂, total carbon dioxide; BE, base excess; PT, prothrombin time; PTT, partial thromboplastin time; INR, international normalized ratio; ALT, glutamic pyruvic transaminase; AST, glutamic oxaloacetic transaminase; ALP, alkaline phosphatase; TBIL, total bilirubin; urea, blood urea nitrogen; P, serum inorganic phosphorus; Cl, chloride; AG, anion gap; o₂_flow, oxygen flow rate; peep, positive end-expiratory pressure; fio₂, fraction of inspiration oxygen; flow_rate, oxygen delivery rate; A1c, glycosylated hemoglobin; TG, total triglycerides; HDL, high density lipoprotein; LDL, low density lipoprotein; LD, lactic dehydrogenase; CK, creatine kinase; CKMB,

Supplementary Figure 3 ROC curves of all screened variables



Footnote to Supplementary Figure 3: BMI, body mass index; meanbp, mean blood pressure; resprate, respiratory rate; temp, temperature; spo2, oxygen saturation of blood; WBC, white blood cells; RBC, red blood cells; MCH, mean corpuscular hemoglobin; MCHC, mean corpuscular hemoglobin concentration; MCV, mean corpuscular volume; RDW, red blood cell distribution width; RDW-SD, red blood cell distribution width-standard deviation; po2, partial pressure of oxygen; pco2, partial pressure of carbon dioxide; pH, potential of hydrogen; Na, sodium; K, potassium; Ca, calcium; totalco2, total carbon dioxide; BE, base excess; PT, prothrombin time; PTT, partial thromboplastin time; INR, international normalized ratio; ALT, glutamic pyruvic transaminase; AST, glutamic oxaloacetic transaminase; ALP, alkaline phosphatase; TBIL, total bilirubin; urea, blood urea nitrogen; P, serum inorganic phosphorus; Cl, chloride; AG, anion gap; o2_flow, oxygen flow rate; peep, positive end-expiratory pressure; fio2, fraction of inspiration oxygen; flow_rate, oxygen delivery rate

Supplementary Figure 4 Heatmap involving all screened variables

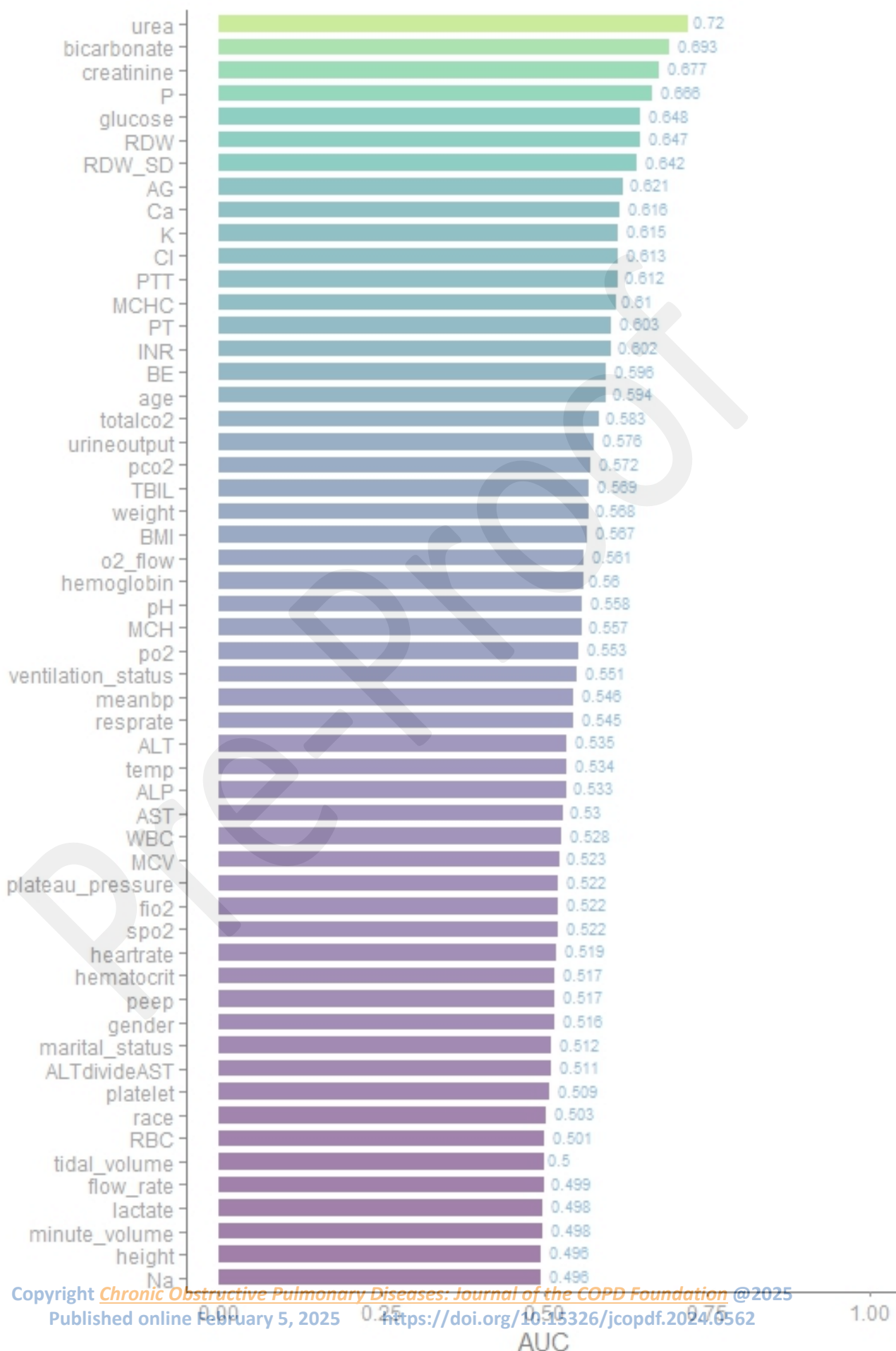


Footnote to Supplementary Figure 4: BMI, body mass index; meanbp, mean blood pressure; resprate, respiratory rate; temp, temperature; spo2, oxygen saturation of blood; WBC, white blood cells; RBC, red blood cells; MCH, mean corpuscular hemoglobin; MCHC, mean corpuscular hemoglobin concentration; MCV, mean corpuscular volume; RDW, red blood cell distribution width; RDW-SD, red blood cell distribution width-standard deviation; po2, partial pressure of oxygen; pco2, partial pressure of carbon dioxide; pH, potential of hydrogen; Na,

sodium; K, potassium; Ca, calcium; totalco2, total carbon dioxide; BE, base excess; PT, prothrombin time; PTT, partial thromboplastin time; INR, international normalized ratio; ALT, glutamic pyruvic transaminase; AST, glutamic oxaloacetic transaminase; ALP, alkaline phosphatase; TBIL, total bilirubin; urea, blood urea nitrogen; P, serum inorganic phosphorus; Cl, chloride; AG, anion gap; o2_flow, oxygen flow rate; peep, positive end-expiratory pressure; fio2, fraction of inspiration oxygen; flow_rate, oxygen delivery rate

Supplementary Figure 5 AUC histogram involving all screened variables

Pre-proof



Footnote to Supplementary Figure 5: BMI, body mass index; meanbp, mean blood pressure; resprate, respiratory rate; temp, temperature; spo2, oxygen saturation of blood; WBC, white blood cells; RBC, red blood cells; MCH, mean corpuscular hemoglobin; MCHC, mean corpuscular hemoglobin concentration; MCV, mean corpuscular volume; RDW, red blood cell distribution width; RDW-SD, red blood cell distribution width-standard deviation; po2, partial pressure of oxygen; pco2, partial pressure of carbon dioxide; pH, potential of hydrogen; Na, sodium; K, potassium; Ca, calcium; totalco2, total carbon dioxide; BE, base excess; PT, prothrombin time; PTT, partial thromboplastin time; INR, international normalized ratio; ALT, glutamic pyruvic transaminase; AST, glutamic oxaloacetic transaminase; ALP, alkaline phosphatase; TBIL, total bilirubin; urea, blood urea nitrogen; P, serum inorganic phosphorus; Cl, chloride; AG, anion gap; o2_flow, oxygen flow rate; peep, positive end-expiratory pressure; fio2, fraction of inspiration oxygen; flow_rate, oxygen delivery rate