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Predictive validity of the sequential organ failure assessment score for mortality in patients with acute respiratory distress syndrome in Vietnam

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Evaluating the prognosis of ARDS patients using grading systems can enhance treatment decisions. This retrospective observational study evaluated the predictive accuracy of the SOFA score, APACHE II score, SpO_2/FiO_2 ratio, and PaO_2/FiO_2 ratio for mortality in ARDS patients in Vietnam. The study included 335 adult ARDS patients admitted to a central hospital from August 2015 to August 2023. Among them, 66.9% were male, the median age was 55 years, and 61.5% died in the hospital. The SOFA (AUROC: 0.651) and APACHE II scores (AUROC: 0.693) showed poor discriminatory ability for hospital mortality. The SpO_2/FiO_2 (AUROC: 0.595) and PaO_2/FiO_2 ratios (AUROC: 0.595) also displayed poor discriminatory ability. In multivariable analyses, after adjusting for the same set of confounding variables, the APACHE II score (adjusted OR: 1.152), SpO_2/FiO_2 ratio (adjusted OR: 0.985), and PaO_2/FiO_2 ratio (adjusted OR: 0.989) were independently associated with hospital mortality. Although the SOFA score (adjusted OR: 1.132) indicated a potential association with hospital mortality, it did not reach statistical significance ($p = 0.081$). However, a SOFA score of ≥10 emerged as an independent predictor (adjusted OR: 3.398) of hospital mortality. These findings emphasize the need for further studies to develop more accurate scoring systems for predicting outcomes in ARDS patients.

Keywords Acute respiratory distress syndrome (ARDS), APACHE II score, Berlin definition criteria, Critical care, Mechanical ventilation, Mortality, New global definition, PaO_2/FiO_2 ratio, SOFA score, SpO_2/FiO_2 ratio

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Acute respiratory distress syndrome (ARDS) is a severe respiratory failure characterized by the acute onset of bilateral alveolar opacities and hypoxemia[1]. Despite advancements in critical care, ARDS has a high mortality rate. A multicentre, international cohort study of 3022 ARDS patients reported a hospital death rate of 40.1% (952/2377)[2].Mortality increases with disease severity, with early deaths often due to the underlying cause of ARDS[3], while later deaths are commonly due to nosocomial pneumonia and sepsis[4]. Respiratory failure is a rare cause of death in ARDS patients[5].

Predicting mortality in ARDS is challenging because it is difficult to distinguish deaths caused by ARDS from those due to comorbidities[6,7]. Factors influencing mortality include age, comorbidities, poor nutrition, severe ARDS, infection, and multi-organ failure (MOF). Treatment depends on disease severity, making it essential to assess ARDS severity scores promptly. Various grading systems are used for this purpose, with the most recognized one being the grading system proposed by the ARDS Definition Task Force[8–11]. However, there is a cautionary note regarding the reliability of the ratio of the arterial oxygen partial pressure to the fraction of inspiratory oxygen concentration (PaO_2/FiO_2ratio)[12], which may lead to inconsistent data[13,14]. Most ARDS deaths result from sepsis or MOF rather than primary pulmonary causes. The Acute Physiology and Chronic Health Evaluation II (APACHE II) score[15], used in intensive care units (ICUs), has good predictive value but is complex and has limitations[15–17]. The Sepsis-3 Task Force's Sequential Organ Failure Assessment (SOFA) score[18,19], indicating sepsis with a 2-point increase, is validated mainly in high-income countries (HICs)[20–24], and its applicability in varied settings is uncertain.

Vietnam, a lower middle-income country (LMIC) with a population of 96.462 million, faces frequent emerging infectious diseases such as severe acute respiratory syndrome coronavirus 1 (SARS-CoV-1)[25], avian influenza A(H5N1)[26,27], and coronavirus disease 2019 (COVID-19)[28,29]. Other more significant causes of sepsis in Vietnamese ICUs include severe dengue[30], *Streptococcus suis*infections[31], malaria[32], and antibiotic resistance[33,34]. Pneumonia and sepsis are the leading causes of ARDS in Vietnam[29,35,36]. Despite economic growth, Vietnam struggles with resource limitations and adequate ARDS management strategies[35,37]. Central hospitals often handle cases that local hospitals cannot manage[38], leading to delays in diagnosis, prognosis, and treatment, including intubation and mechanical ventilation.

In resource-limited settings, accurate scoring systems are crucial for identifying ARDS patients at risk of death and making informed treatment decisions. This study, therefore, aimed to investigate mortality rates and compare the predictive accuracy of the SOFA score, PaO_2/FiO_2 ratio, and APACHE II score for mortality in ARDS patients in Vietnam.

Methods

Source of data

This retrospective observational study is the major update of our published previous study[35], which collected data on all ARDS patients admitted to the Bach Mai Hospital (BMH) in Hanoi, Vietnam, between August 2015 and August 2017, to elucidate the clinical epidemiology and disease prognosis in ARDS patients in Vietnam[35]. To further investigate the mortality rate and compare the predictive accuracy of the SOFA score with the PaO_2/FiO_2 ratio and the APACHE II score for mortality in ARDS patients, we continued to collect retrospective data on these patients admitted to the BMH between September 2017 and August 2023. Subsequently, we merged the data sets from the two stages of data collection at this hospital. It is worth noting that the BMH is designated as a central general hospital with 3,200 beds in northern Vietnam by the Ministry of Health (MOH). In the healthcare system of Vietnam, the central hospitals (level I) are responsible for training hospital staff and treating patients who are unable to be adequately treated in local hospital settings, including provincial and district hospitals (levels II and III, according to the MOH of Vietnam).

Participants

This study included all patients aged 18 years or older who received a diagnosis of ARDS at BMH. The ARDS diagnosis was established by expert clinicians at the study site. The diagnosis of ARDS was based on the Berlin criteria[8,9], which encompass: (i) *Timing*: The onset should occur within one week following a recognized clinical insult or the emergence or aggravation of respiratory symptoms; (ii) *Chest imaging*: The presence of bilateral opacities on imaging that cannot be entirely attributed to effusions, collapse of a lobe or the entire lung, or nodules; (iii) *Oedema origin*: The respiratory failure should not be completely explainable by cardiac failure or excess fluid. An objective evaluation, such as echocardiography, is required to rule out hydrostatic oedema in the absence of any risk factors; and (iv) *Oxygenation*: The oxygenation criterion requires a PaO_2/FiO_2 ratio of ≤ 300 mmHg, with the patient receiving at least 5 cmH_2O of positive end-expiratory pressure (PEEP).

Data collection

We utilized the unified case record form (CRF) to collect data on common types of variables from medical records. We used the EpiData Entry software (EpiData Association, Denmark, Europe) to enter data into the study database, which allowed for simple or programmed data entry and documentation that could prevent data entry errors or mistakes. We did not enter patient identifiers into the database to protect patient confidentiality.

Outcome measures

The primary outcome was hospital mortality, which we defined as death from any cause during the hospitalization. We also examined the secondary outcomes, such as complications and hospital lengths of stay (LOS).

Predictor measures

We defined exposure variables as the SOFA score and APACHE II score, measured from admission up to 24 h later. We also defined the worst peripheral oxygen saturation (SpO_2) to FiO2 (SpO2/FiO2) and PaO_2/FiO_2 ratios on the 1st-day of admission as exposure variables. The SOFA score assesses the severity of organ dysfunction and predicts mortality in critically ill patients[20]. It includes six components: the respiratory system (e.g., PaO2/FiO2 ratio), cardiovascular system (e.g., amount of vasoactive medication necessary to prevent hypotension), hepatic system (e.g., serum bilirubin level), coagulation system (e.g., platelet concentration), neurological system (e.g., Glasgow coma score (GCS)), and renal system (e.g., serum creatinine or urine output). Each component is scored from 0 (indicating normal function) to 4 (indicating severe abnormalities), with the total SOFA score varying from 0 (optimal) to 24 (most severe), where higher scores indicate greater severity[20]. The APACHE II score is used to gauge disease severity in ICUs, calculated from twelve physiological variables and two disease-related factors. Scores range from 0 to 71 points, with higher scores indicating more severe conditions[15]. For score calculations, we used the worst values for each parameter within the 24-hour window. Missing values were addressed by averaging the results immediately preceding and following the missing data. We also used the assumed GCS to estimate the neurological status of sedated patients.

We determined confounding factors as variables collected on the same unified CRF by a fully trained clinician. The CRF contained four sections, which included variables mainly based on the Evidence-Based Clinical Practice Guidelines on the Use of Mechanical Ventilation in Adult Patients with Acute Respiratory Distress Syndrome[39] such as information on:

(i) The first section focused on baseline characteristics, such as inter-hospital care (e.g., prior hospitalization, inter-hospital transportation, inter-hospital care provider, inter-hospital airway, and respiratory care during the transport), demographics (i.e., age and gender), documented comorbidities (e.g., cerebrovascular disease, chronic cardiac failure, coronary artery disease (CAD)/myocardial infarction (MI), hypertension, chronic obstructive pulmonary disease (COPD)/asthma, other chronic pulmonary diseases, tuberculosis, active neoplasm, chronic renal failure, ulcer disease, diabetes mellitus, immunoincompetence, and haematological disease), and details of admission. We also used the 19 comorbidity categories to compute the Charlson Comorbidity Index (CCI) score, which measures the predicted mortality rate based on the presence of comorbidities[40]. A score of zero indicates that no comorbidities were detected; the higher the score, the higher the expected mortality rate is[40–42].

(ii) The second section comprised characteristics upon admission, such as vital signs (e.g., heart rate (HR), respiration rate (RR), arterial blood pressure (BP), and body temperature), laboratory parameters (e.g., white blood cells (WBCs), haemoglobin, platelet, C-reactive protein (CRP), urea, creatinine, glucose, albumin, ferritin, and interleukin-6 (IL-6)), chest X-ray (CXR) findings (e.g., bilateral opacities and number of involved quadrants), arterial blood gases (ABGs) (e.g., PaO_2, $PaCO_2$, the blood potential hydrogen (pH), and PaO_2/FiO_2 ratio), and respiratory pathogens (e.g., influenza A(H1N1) virus, cytomegalovirus (CMV), influenza B virus, and parainfluenza virus). In the study site, virus infection was confirmed by a positive real-time reverse transcription-polymerase chain reaction test using samples obtained from the respiratory tract by nasopharyngeal swab, throat or mouth swab, or tracheal lavage fluid.

(iii) The third section captured life-sustaining treatments provided during the ICU stay, such as respiratory support on the first day of admission (e.g., oxygen supplements and MV) and adjunctive therapies (e.g., prone positioning, recruitment manoeuvres, extracorporeal membrane oxygenation (ECMO), antiviral drugs, antibiotics, corticosteroids, heparin, antiplatelet drugs, novel oral anticoagulants, continuous sedation, continuous neuromuscular blocking agents (NMBAs), renal replacement therapy (RRT), extracorporeal cytokine adsorption therapy (ECAT), tracheostomy, and inhaled vasodilators).

(iv) The fourth section focused on documenting complications (e.g., hospital-acquired pneumonia (HAP), secondary bacterial infections, septic shock, MOF, deep venous thrombosis (DVT), gastrointestinal bleeding, and pneumothorax) and clinical outcomes (e.g., hospital mortality). HAP was defined as pneumonia that developed 48 h or more after admission and did not appear to be incubating at the time of admission[43]. Additionally, septic shock was identified as a clinical construct of sepsis characterized by persisting hypotension requiring vasopressors to maintain a mean arterial pressure ≥ 65 mmHg, along with a serum lactate level > 2 mmol/L (18 mg/dL) despite adequate volume resuscitation[18].

Sample size

In this retrospective observational study, the primary outcome was hospital mortality. Therefore, we used the formula to find the minimum sample size for estimating a population proportion with a confidence level of 95%, a confidence interval (margin of error) of ± 5.35%, and an assumed population proportion of 47.8%, based on the hospital mortality rate (47.8%) reported in a previously published study[44]. As a result, our sample size should be at least 335 patients, which might be large enough to reflect a normal distribution.

$$n = \frac{z^2 x\, \widehat{p}\,(1-\widehat{p})}{\epsilon^{\,2}}$$

where:

z is the z score (z score for a 95% confidence level is 1.96)
ε is the margin of error (ε for a confidence interval of ± 5.35% is 0.0535)
$\widehat{p}$ is the population proportion ($\widehat{p}$ for a population proportion of 47.8% is 0.478)
n is the sample size

Statistical analyses

We used IBM® SPSS® Statistics 22.0 (IBM Corp., Armonk, United States of America) and Analyse-it statistical software (Analyse-it Software, Ltd., Leeds, United Kingdom) for data analysis. We report the data as numbers (no.) and percentages (%) for categorical variables and medians and interquartile ranges (Q1–Q3) or means and standard deviations (SDs) for continuous variables. Furthermore, comparisons were made between survival and death in the hospital for each variable using the Chi-squared or Fisher's exact test for categorical variables and the Mann–Whitney U test, Kruskal–Wallis test, or one-way analysis of variance for continuous variables.

To predict hospital mortality among ARDS patients upon admission, we plotted Receiver Operating Characteristic (ROC) curves and calculated Areas Under the ROC curves (AUROC) to determine the discriminatory ability of the SOFA and APACHE II scores. In this analysis, a higher score indicates a more positive test result. Additionally, we examined the SpO_2/FiO_2 and PaO_2/FiO_2 ratios, where a lower ratio signifies a more positive test result. To compare the AUROCs, we used Z-statistics to evaluate the differences in the AUROC between the SOFA and APACHE II scores and between the SpO_2/FiO_2 and PaO_2/FiO_2 ratios in predicting hospital mortality. Additionally, the optimal cut-off value of each score or ratio was determined by ROC curve analysis and defined as the point with the maximum value of Youden's index (i.e., sensitivity + specificity − 1). Based on these cut-off values, patients were categorized into two severity groups: those with scores below the cut-off value and those with scores at or above the cut-off value. Finally, we calculated correlation coefficients (Rs) using Spearman's rho to explore the relationship between the severity scoring systems upon admission.

We assessed the factors associated with deaths in the hospital using logistic regression analysis. To reduce the number of predictors and the multicollinearity issue and resolve the overfitting, we used different methods to select variables as follows: *First*, we put all variables of inter-hospital care, demographics, documented comorbidities, clinical and laboratory features, ABGs, CXR findings, severity of illness, oxygen supplement, MV, adjunctive therapies, and complications into the univariable logistic regression model; *Next*, we selected variables if the P-value was < 0.05 in the univariable analysis between death and survival in the hospital, as well as those that are clinically crucial, to put in the multivariable logistic regression models. These variables comprised an exposure variable (e.g., SOFA score, SpO_2/FiO_2 ratio, PaO_2/FiO_2 ratio, APACHE II score, SOFA score ≥ cut-off value, or APACHE II score ≥ cut-off value) and a set of confounding factors. The confounding factors included inter-hospital care (i.e., MV applied in prior hospitalization, inter-hospital transport, and inter-hospital airway), demographics (i.e., age, gender), documented comorbidities (i.e., CCI score), adjunctive therapies (i.e., prone positioning, recruitment manoeuvres, antiviral drugs, corticosteroids, NMBAs, and ECAT), and complications (i.e., HAP, acute kidney injury, and septic shock); *Final*, using a stepwise backward elimination method, we started with each full multivariable logistic regression model that included an exposure variable and the same set of confounding factors. This method then deleted the least statistically significant variables stepwise from each full model until all remaining variables were independently associated with hospital mortality in each final model. We presented the odds ratios (ORs) and 95% confidence intervals (CIs) in the univariable logistic regression model and the adjusted ORs (AORs) and 95% CIs in the multivariable logistic regression model.

The significance levels were two-tailed for all analyses, and we considered the $P < 0.05$ as a statistically significant value.

Ethical issues

The Bach Mai Hospital Scientific and Ethics Committees approved this study (approval number: 6576/QD–BM; research code: BM_2023_160). The study was conducted following the Declaration of Helsinki. The Bach Mai Hospital Scientific and Ethics Committees waived the need for informed consent for this retrospective observational study. Public notification of this study was made by public posting, according to the Transparent Reporting of a multivariable prediction model for Individual Prognosis or Diagnosis (TRIPOD) statement for reporting a study developing or validating a multivariable prediction model for diagnosis or prognosis. All data analyses were based on datasets kept in password-protected systems, and all final presented data have been anonymized.

Results

In our study, we input data from 374 ARDS patients into the database. However, we excluded five patients who were under 18 years old. Additionally, we removed thirty patients due to missing data for most variables (8.1%; 30/369). Furthermore, four duplicate entries were also eliminated (1.1%; 4/369). As a result, our analyses included 335 eligible patients (Fig. 1).

Clinical characteristics and management

In this study, most patients were transferred from local hospitals (89.0%; 298/335) (Table S1 in Additional file 1). Among our cohort, 66.9% (224/335) were male, and the median age was 55.0 years (Q1–Q3: 39.0–66.0) (Table 1). Nearly half of the patients exhibited smoking habits, including those who had quit (14.0%, 30/214) and those who were current smokers (29.9%, 64/214) (Table S2 in Additional file 1). Commonly documented comorbidities included hypertension (29.9%, 67/224), diabetes mellitus (20.1%, 45/224), chronic renal failure (9.6%, 22/228), haematological diseases (6.1%, 14/228), and COPD/asthma (5.8%, 13/224) (Table 1). The primary aetiology of ARDS was pneumonia (91.1%, 204/224) (Table 2), with the predominant pathogens being influenza A(H1N1) virus (12.5%, 28/224), CMV (2.8%; 6/218), influenza B virus (1.8%; 4/224), and parainfluenza virus (1.3%; 3/224) (Table S3 in Additional file 1). Among all patients, the mean SpO_2/FiO_2 ratio was 120.81 (SD: 45.54), while the mean PaO_2/FiO_2 ratio was 109.07 (SD: 56.28), with the PaO_2/FiO_2 ratio of ≤ 100 mmHg that was most commonly observed (57.4%, 187/326) (Table 3). Additionally, the median SOFA score was 10.0 (Q1–Q3: 7.0–12.0), and the median APACHE II score was 18.0 (Q1–Q3: 13.0–23.0) from admission up to 24 h later (Table 3). Most patients (95.6%; 304/318) received invasive MV on the first day of admission (Table 4). Furthermore,

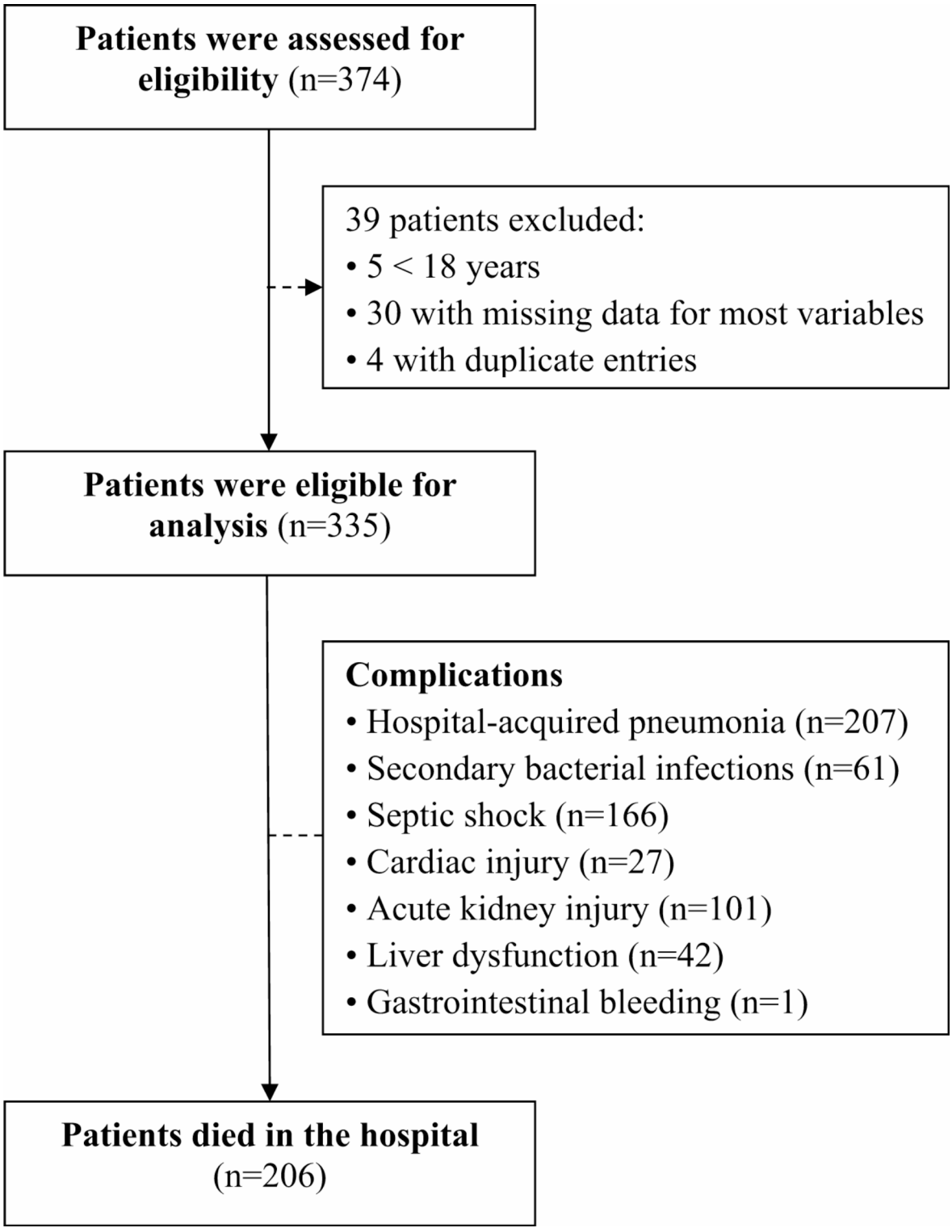

Fig. 1. Flowchart of the study design.

24.8% (82/330) of patients underwent prone positioning, and 17.7% (59/333) utilized recruitment manoeuvres while on MV (Table 4). A majority of patients (100%; 138/138) received RRT, and 36.9% (73/198) underwent ECAT during the ICU stay (Table 4). We also conducted analyses to compare the clinical characteristics and management between patients who survived and those who died in the hospital, as shown in Tables 1, 2, 3 and 4 and Tables S1 to S6 in Additional file 1.

Variables	All cases $n=335$	Survived $n=129$	Died $n=206$	*P* value[a]
Demographics				
Age (year), median (Q1-Q3)	55.0 (39.0–66.0)	46.0 (35.0–61.5)	57.0 (43.0–69.0)	< 0.001
Gender (male), no. (%)	224 (66.9)	83 (64.3)	141 (68.4)	0.437
Comorbidities				
Cerebrovascular disease, no. (%)	5 (1.5)	0 (0.0)	5 (2.4)	0.161
Chronic cardiac failure, no. (%), $n=230$	9 (3.9)	2 (2.4)	7 (4.7)	0.496
CAD/MI, no. (%), $n=219$	4 (1.8)	0 (0.0)	4 (2.8)	0.300
Hypertension, no. (%), $n=224$	67 (29.9)	25 (30.9)	42 (29.4)	0.815
COPD/asthma, no. (%), $n=224$	13 (5.8)	0 (0.0)	13 (9.1)	0.005
Other CPD, no. (%), $n=331$	24 (7.3)	12 (9.4)	12 (5.9)	0.237
Tuberculosis, no. (%), $n=224$	5 (2.2)	1 (1.2)	4 (2.8)	0.656
Active neoplasm, no. (%), $n=224$	11 (4.9)	2 (2.5)	9 (6.3)	0.335
Chronic renal failure, no. (%), $n=228$	22 (9.6)	11 (13.6)	11 (7.5)	0.136
Ulcer disease, no. (%), $n=334$	12 (3.6)	4 (3.1)	8 (3.9)	0.773
Diabetes mellitus, no. (%), $n=224$	45 (20.1)	16 (19.8)	29 (20.3)	0.925
Immunoincompetence, no. (%), $n=228$	14 (6.1)	7 (8.4)	7 (4.9)	0.292
Haematological disease, no. (%), $n=228$	14 (6.1)	3 (3.7)	11 (7.5)	0.242
CCI, median (Q1-Q3), $n=148$	3.0 (1.0–5.0)	2.0 (1–4.75)	3.0 (1.0–5.0)	0.369

Table 1. Demographics and comorbidities of patients with acute respiratory distress syndrome, according to hospital survivability. [a]To indicate comparisons between patients who survived and those who died in the hospital. CAD, coronary artery disease; CCI, Charlson Comorbidity Index; COPD, chronic obstructive pulmonary disease; CPD, chronic pulmonary disease; MI, myocardial infarction; no., number of patients; Q, quartile.

Variables	All cases $n=335$	Survived $n=129$	Died $n=206$	*P* value[a]
Aetiology of ARDS				
Pneumonia, no. (%), $n=224$	204 (91.1)	68 (84.0)	136 (95.1)	0.005
Aspiration of gastric contents, no. (%), $n=223$	4 (1.8)	1 (1.2)	3 (2.1)	> 0.999
Pulmonary contusion, no. (%), $n=222$	2 (0.9)	1 (1.3)	1 (0.7)	> 0.999
Inhalation injury, no. (%), $n=223$	3 (1.3)	2 (2.5)	1 (0.7)	0.299
Pulmonary vasculitis, no. (%), $n=223$	1 (0.4)	1 (1.2)	0 (0.0)	0.363
Drowning, no. (%), $n=224$	9 (4.0)	7 (8.6)	2 (1.4)	0.012
Clinical characteristics				
HR (beats/min), median (Q1-Q3), $n=224$	123.0 (105.0–135.0)	124.0 (104.5–133.5)	123.0 (106.0–138.0)	0.549
RR (breaths/min), median (Q1-Q3), $n=224$	26.0 (22.0–30.75)	25.0 (20.0–30.0)	28.0 (23.0–32.0)	0.157
Systolic BP (mmHg), mean (SD), $n=224$	106.81 (24.82)	111.70 (21.53)	104.04 (26.17)	0.022
Diastolic BP (mmHg), mean (SD), $n=224$	62.85 (15.220	66.85 (12.95)	60.59 (15.97)	0.005
Body temperature (°C), mean (SD), $n=224$	37.84 (1.04)	37.69 (0.90)	37.92 (1.11)	0.174
Laboratory investigations				
WBCs ($x10^9$/L), mean (SD)	14.59 (12.34)	12.73 (7.68)	15.76 (14.41)	0.099
Haemoglobin (g/L), mean (SD), $n=224$	115.88 (25.24)	115.05 (23.02)	116.35 (26.49)	0.716
Platelet count ($x10^9$/L), mean (SD)	177.65 (116.69)	175.28 (97.17)	179.13 (127.60)	0.535
Ure (mmol/L), mean (SD), $n=224$	11.96 (9.53)	9.67 (7.53)	13.26 (10.30)	0.001
Creatinine (μmol/L), mean (SD)	152.07 (150.09)	138.05 (127.04)	160.84 (162.56)	0.059

Table 2. Clinical and laboratory characteristics of patients with acute respiratory distress syndrome upon admission, according to hospital survivability. [a]To indicate comparisons between patients who survived and those who died in the hospital. BP, blood pressure; HR, heart rate; no., number of patients; Q, quartile; RR, respiration rate; SD, standard deviation; WBCs, white blood cells.

Primary and secondary outcomes

Of the 335 eligible patients, 206 (61.5%) died in the hospital (Fig. 1), and the mean LOS was 10.38 (SD: 11.70) days (Table 4). During the study, patients with ARDS experienced several common complications, including HAP (61.8%; 207/335), secondary bacterial infections (18.2%; 61/335), septic shock (49.6%; 166/335), acute

Variables	All cases $n=335$	Survived $n=129$	Died $n=206$	*P* value[a]
Arterial blood gas				
pH, mean (SD), $n=334$	7.31 (0.16)	7.35 (0.12)	7.29 (0.17)	0.004
PaO_2 (mmHg), mean (SD), $n=333$	81.91 (35.35)	89.36 (41.16)	77.19 (30.30)	0.028
$PaCO_2$ (mmHg), mean (SD), $n=334$	44.46 (16.28)	43.45 (14.54)	45.09 (17.29)	0.528
FiO_2 (%),mean (SD), $n=327$	81.82 (21.49)	79.40 (22.36)	83.29 (20.86)	0.138
PaO_2/FiO_2 ratio, mean (SD), $n=326$	109.07 (56.28)	123.75 (65.07)	100.06 (48.12)	0.004
SpO_2 (%), mean (SD), $n=331$	89.72 (7.91)	91.63 (7.21)	88.51 (8.11)	< 0.001
SpO_2/FiO_2 ratio, mean (SD) $n=324$	120.81 (45.54)	128.45 (47.25)	116.13 (43.92)	0.004
Severity of illness				
SOFA score, median (Q1-Q3)	10.0 (7.0–12.0)	8.0 (6.0–11.0)	10.0 (7.0–12.0)	< 0.001
APACHE II score, median (Q1-Q3), $n=333$	18.0 (13.0–23.0)	15.0 (10.5–20.0)	20.0 (15.0–25.0)	< 0.001
Berlin definition, no. (%), $n=326$				0.007
$PaO_2/FiO_2 > 300$ mmHg	0 (0.0)	0 (0.0)	0 (0.0)	
200 mmHg $< PaO_2/FiO_2 \leq 300$ mmHg	26 (8.0)	16 (12.9)	10 (5.0)	
100 mmHg $< PaO_2/FiO_2 \leq 200$ mmHg	113 (34.7)	48 (38.7)	65 (32.2)	
$PaO_2/FiO_2 \leq 100$ mmHg	187 (57.4)	60 (48.4)	127 (62.9)	

Table 3. Blood gas exchange and severity of patients with acute respiratory distress syndrome upon admission, according to hospital survivability. [a] To indicate comparisons between patients who survived and those who died in the hospital. APACHE II score, Acute Physiology and Chronic Health Evaluation II score; $PaCO_2$, arterial carbon dioxide partial pressure; PaO_2, arterial oxygen partial pressure; pH, blood potential hydrogen; no., number of patients; SD, standard deviation; SOFA score, Sequential Organ Failure Assessment score; SpO_2, peripheral oxygen saturation.

kidney injury (30.1%; 101/335), and liver dysfunction (12.5%; 42/335) (Table 4). Additionally, Table 4 provides a comparison of complications between patients who survived and those who died in the hospital.

Overall predictive performance of severity scoring systems for mortality

Figures 2 and 3, along with Table S7 in Additional File 1, illustrate the overall performance of severity scoring systems in predicting hospital mortality. Figure 2 shows a positive correlation between scores and hospital mortality, indicating that these scores had poor discriminatory ability for hospital mortality. Specifically, the SOFA score demonstrated an AUROC of 0.651 (95% CI: 0.591–0.710) with a cut-off value of ≥ 9.5. This score achieved a sensitivity of 60.7% and a specificity of 63.6% (P_{AUROC} <0.001). Similarly, the APACHE II score exhibited a higher AUROC of 0.693 (95% CI: 0.636–0.750) with a cut-off value of ≥ 19.5, yielding a sensitivity of 55.4% and a specificity of 74.4% (P_{AUROC} <0.001). However, there was no significant difference between the AUROC curves of the SOFA and APACHE II scores (AUROC difference: −0.042; 95% CI: −0.105–0.021; Z-statistic: −1.32; $p=0.188$) (Table S8 in Additional File 1). Conversely, the SpO_2/FiO_2 and the PaO_2/FiO_2 ratios were inversely associated with hospital mortality (Fig. 3), indicating poor discriminatory ability for hospital mortality. The SpO_2/FiO_2 ratio displayed an AUROC of 0.595 (95% CI: 0.531–0.658) with a cut-off value of ≥ 90.50, resulting in a sensitivity of 35.3% and a specificity of 79.7% (P_{AUROC} = 0.004). Similarly, the PaO_2/FiO_2 ratio also yielded an AUROC of 0.595 (95% CI: 0.529–0.660) with a cut-off value of ≥ 45.40, achieving a sensitivity of 76.2% and a specificity of 46.0% (P_{AUROC} = 0.004).

Association of severity scoring systems with mortality

In the univariable logistic regression analyses (Table 5, as well as Tables S9 to S14 in Additional file 1), the SOFA score exhibited a significant association with hospital mortality, yielding an OR of 1.168 (95% CI: 1.093–1.250; $p<0.001$). Similarly, the APACHE II score demonstrated a significant association with hospital mortality, with an OR of 1.109 (95% CI: 1.070–1.149; $p<0.001$). Additionally, both the SpO_2/FiO_2 ratio (OR: 0.994; 95% CI: 0.989–0.999; $p=0.019$) and the PaO_2/FiO_2 ratio (OR: 0.993; 95% CI: 0.989–0.997; $p<0.001$) were significantly associated with hospital mortality. However, in the multivariable logistic regression analyses (Table 5, as well as Tables S9 to S14 in Additional file 1), after adjusting for the same set of confounding variables, only the APACHE II score (AOR: 1.152; 95% CI: 1.064–1.248; $p<0.001$), the SpO_2/FiO_2 ratio (AOR: 0.985; 95% CI: 0.973–0.996; $p=0.010$), and the PaO_2/FiO_2 ratio (AOR: 0.989; 95% CI: 0.980–0.997; $p=0.009$) remained independently associated with hospital mortality. While the SOFA score (AOR: 1.132; 95% CI: 0.985–1.301; $p=0.081$) indicated a potential association with hospital mortality, it did not reach statistical significance. Notably, a SOFA score of ≥ 10 emerged as an independent predictor of hospital mortality (AOR: 3.398; 95% CI: 1.300–8.880; $p=0.013$).

Discussion

In this study, over two-thirds of ARDS patients died in the hospital (Fig. 1). Both the SOFA and APACHE II scores demonstrated poor ability to predict hospital mortality upon admission; a positive correlation was observed between these scores and hospital mortality (Fig. 2 and Table S7 in Additional file 1). In contrast,

Variables	All cases $n=335$	Survived $n=129$	Died $n=206$	P value[a]
Respiratory support				
The first day respiratory support, $n=318$				0.918
Oxygen only, no. (%)	7 (2.2)	3 (2.5)	4 (2.0)	
Non-invasive, no. (%)	7 (2.2)	2 (1.7)	5 (2.5)	
Invasive, no. (%)	304 (95.6)	115 (95.8)	189 (95.5)	
None of the above, no. (%)	0 (0.0)	0 (0.0)	0 (0.0)	
Adjunctive therapies during ICU stay				
Prone positioning, no. (%), $n=330$	82 (24.8)	24 (18.9)	58 (28.6)	0.048
Recruitment manoeuvres, no. (%), $n=333$	59 (17.7)	19 (14.7)	40 (19.6)	0.256
ECMO, no. (%)	22 (8.8)	9 (9.1)	13 (8.7)	0.908
Antiviral drugs, no. (%), $n=321$	69 (21.5)	39 (30.5)	30 (15.5)	0.001
Antibiotics, no. (%), $n=321$	314 (97.8)	126 (98.4)	188 (97.4)	0.707
Corticosteroids, no. (%), $n=327$	81 (24.8)	33 (26.4)	48 (23.8)	0.591
Continuous sedation, no. (%), $n=334$	320 (95.8)	123 (96.1)	197 (95.6)	0.837
NMBAs, no. (%), $n=331$	240 (72.5)	85 (66.9)	155 (76.0)	0.073
RRT, no. (%), $n=138$	138 (100.0)	46 (100.0)	92 (100.0)	NA
ECAT, no. (%), $n=198$	73 (36.9)	28 (37.8)	45 (36.3)	0.827
Tracheostomy, no. (%), $n=249$	16 (6.4)	12 (12.1)	4 (2.7)	0.003
Inhaled vasodilators, no. (%), $n=224$	1 (0.4)	1 (1.2)	0 (0.0)	0.362
Neutrophil elastase therapy, no. (%), $n=223$	1 (0.4)	1 (1.2)	0 (0.0)	0.359
Clinical time-course				
LOS (day), mean (SD)	10.38 (11.70)	15.67 (13.16)	7.13 (9.34)	<0.001
Complications				
HAP, no. (%)	207 (61.8)	79 (61.2)	128 (62.1)	0.870
Secondary bacterial infections, no. (%)	61 (18.2)	15 (11.6)	46 (22.3)	0.014
Septic shock, no. (%)	166 (49.6)	49 (38.0)	117 (56.8)	0.001
Cardiac injury, no. (%)	27 (8.1)	9 (7.0)	18 (8.7)	0.564
Acute kidney injury, no. (%)	101 (30.1)	30 (23.3)	71 (34.5)	0.030
Liver dysfunction, no. (%)	42 (12.5)	15 (11.6)	27 (13.1)	0.691
Gastrointestinal bleeding, no. (%)	1 (0.3)	1 (0.8)	0 (0.0)	0.385

Table 4. Management and complications of patients with acute respiratory distress syndrome, according to hospital survivability. [a]To indicate comparisons between patients who survived and those who died in the hospital. ECAT, extracorporeal cytokine adsorption therapy; ECMO, extracorporeal membrane oxygenation; HAP, hospital-acquired pneumonia; LOS, hospital lengths of stay; MV, mechanical ventilation; NA, not available; NMBAs, neuromuscular blocking agents; no., number of patients; RRT, renal replacement therapy; SD, standard deviation.

the SpO_2/FiO_2 and PaO_2/FiO_2 ratios exhibited an inverse relationship with hospital mortality, indicating poor discriminatory ability for hospital mortality (Fig. 3 and Table S7 in Additional file 1). The multivariable logistic regression analyses (Table 5, as well as Tables S9 to S14 in Additional file 1) revealed that, after adjusting for the same set of confounding variables, only the APACHE II score, SpO_2/FiO_2 ratio, and PaO_2/FiO_2 ratio were independently associated with hospital mortality. Although the SOFA score indicated a potential association with hospital mortality, it did not reach statistical significance. Notably, a SOFA score of ≥ 10 was identified as an independent predictor of hospital mortality (Table 5 and Table S10 in Additional file 1).

The lack of extensive data on ARDS patients in Vietnam makes comprehensive conclusions difficult. However, the hospital mortality rate from the present study aligns with our previously published rate of 57.1% (72/126)[35]. This consistency is due to identical inclusion criteria and the same hospital setting. In contrast, our observed rate exceeds the rates reported in several other studies: the Validation of Biomarkers in Acute Lung Injury Diagnosis (VALID) study in the United States (US) reported 23.7% (153/646)[45], the Acute Lung Injury: Epidemiology and Natural History (ALIEN) study in Spain reported 47.8% (122/255)[44], and the Large Observational Study to Understand the Global Impact of Severe Acute Respiratory Failure (LUNG SAFE) study reported 40.1% (952/2377)[2]. These disparities may arise from various factors. *First*, most ARDS patients in our study were transferred from local facilities to central hospitals (Table S1in Additional file 1); this resulted in a highly selective cohort, as not all ARDS patients from local facilities were transferred[35,38]. In Vietnam, ARDS patients are initially diagnosed with severe pneumonia at local hospitals and are transferred if their condition worsens[35,38], causing delayed diagnosis and treatment. *Secondly*, transferring ARDS patients can worsen their condition. In the present study, the essential interventions such as intubation (59.7%; 114/191) and invasive MV (24.7%; 39/158) were limited during transfers (Table S1in Additional file 1). A study in the US also found

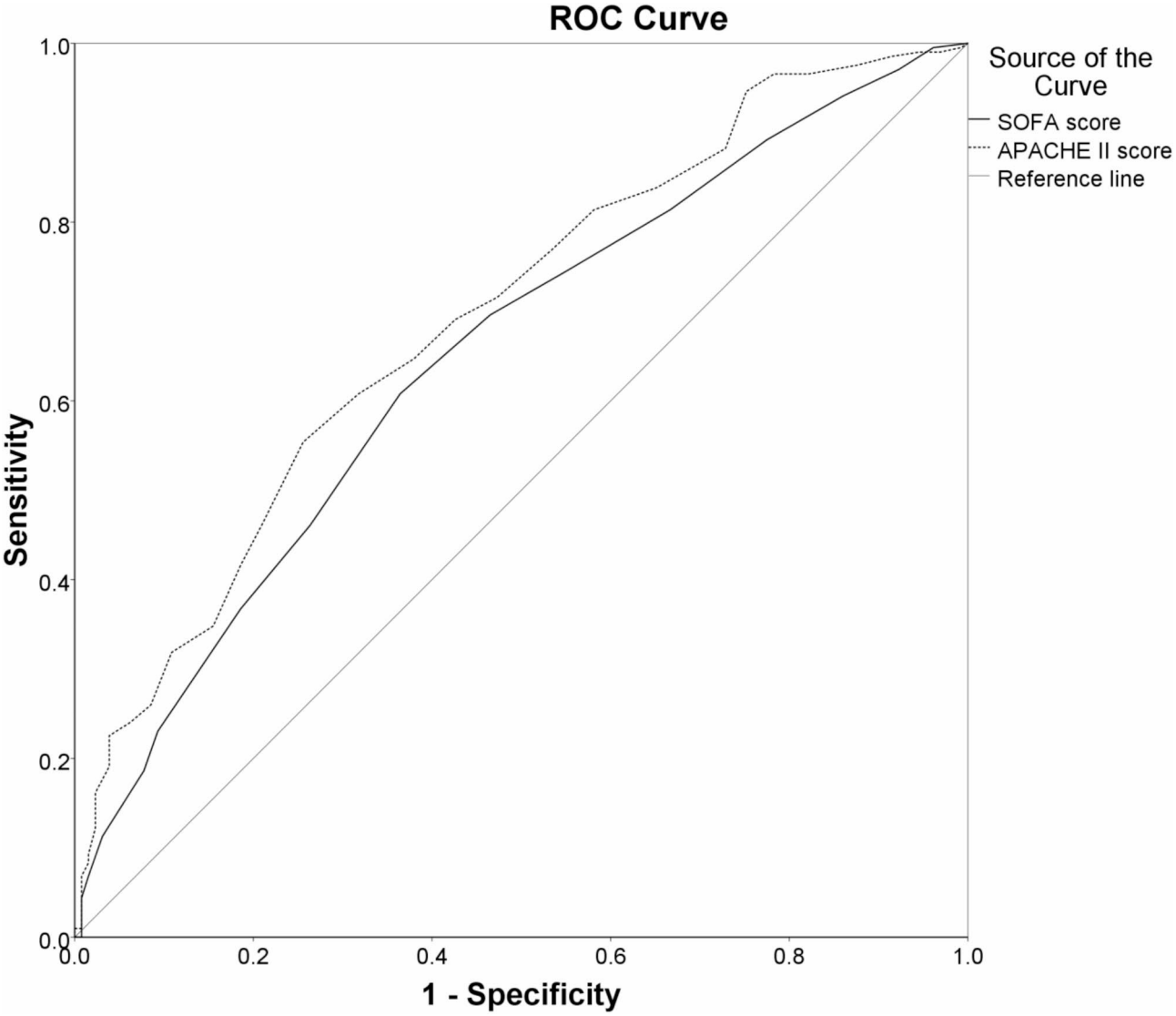

Fig. 2. Overall predictive performance of the SOFA and APACHE II scores for hospital mortality in ARDS patients. The SOFA score had an AUROC of 0.651 (95% CI 0.591–0.710) with a cut-off value of ≥ 9.5, a sensitivity of 60.7%, a specificity of 63.6%, and a PAUROC of < 0.001. Similarly, the APACHE II score showed an AUROC of 0.693 (95% CI 0.636–0.750) with a cut-off value of ≥ 19.5, a sensitivity of 55.4%, a specificity of 74.4%, and a PAUROC of < 0.001. However, both scoring systems exhibited poor discriminatory ability for hospital mortality. A positive correlation was observed between these scores and hospital mortality rates. APACHE II, Acute Physiology and Chronic Health Evaluation II score; ARDS, acute respiratory distress syndrome; AUROC, the area under the receiver operator characteristic curve; CI, confidence interval; SOFA, Sequential Organ Failure Assessment score.

delayed intubation associated with higher mortality[46]. Limited data on patient transfers in Vietnam highlight risk factors for mortality, such as increased transfers and suboptimal care quality[47]. *Finally*, differences in patients, pathogens, and clinical care between LMICs and HICs contribute to observed variations[48–51]. The primary causes of death in ARDS patients are multiple organ dysfunction syndrome, sepsis/septic shock, and pneumonia. While previous studies consistently identify pneumonia as the primary cause of ARDS, such as the VALID (19.3%; 125/646)[45], the ALIEN (42.4%; 108/255)[44], and the LUNG SAFE study (59.4%; 1794/3022)[2], our study even found that nearly all ARDS patients had pneumonia as the primary cause (Table 2). Additionally, the SOFA score in our cohort (Table 3) aligns with the score reported in the LUNG SAFE study (10.1 [95% CI: 9.9–10.2])[2]. However, the PaO_2/FiO_2 ratio (Table 3) is lower than that reported in the LUNG SAFE study (161 mmHg [95% CI: 158–163])[2]. This difference may be due to a higher rate of pneumonia in our study, which was the primary cause of ARDS. Therefore, despite similar illness severity scores between the two studies, our hospital mortality rate is higher. The rate of patients receiving invasive MV in our study (Table 4) is comparable to that in the LUNG SAFE study (84.5%; 2377/2813)[2]. However, a much higher rate of patients in our cohort received NMBAs (Table 4) compared to the LUNG SAFE study (21.7%; 516/2377)[2], possibly due to the lower

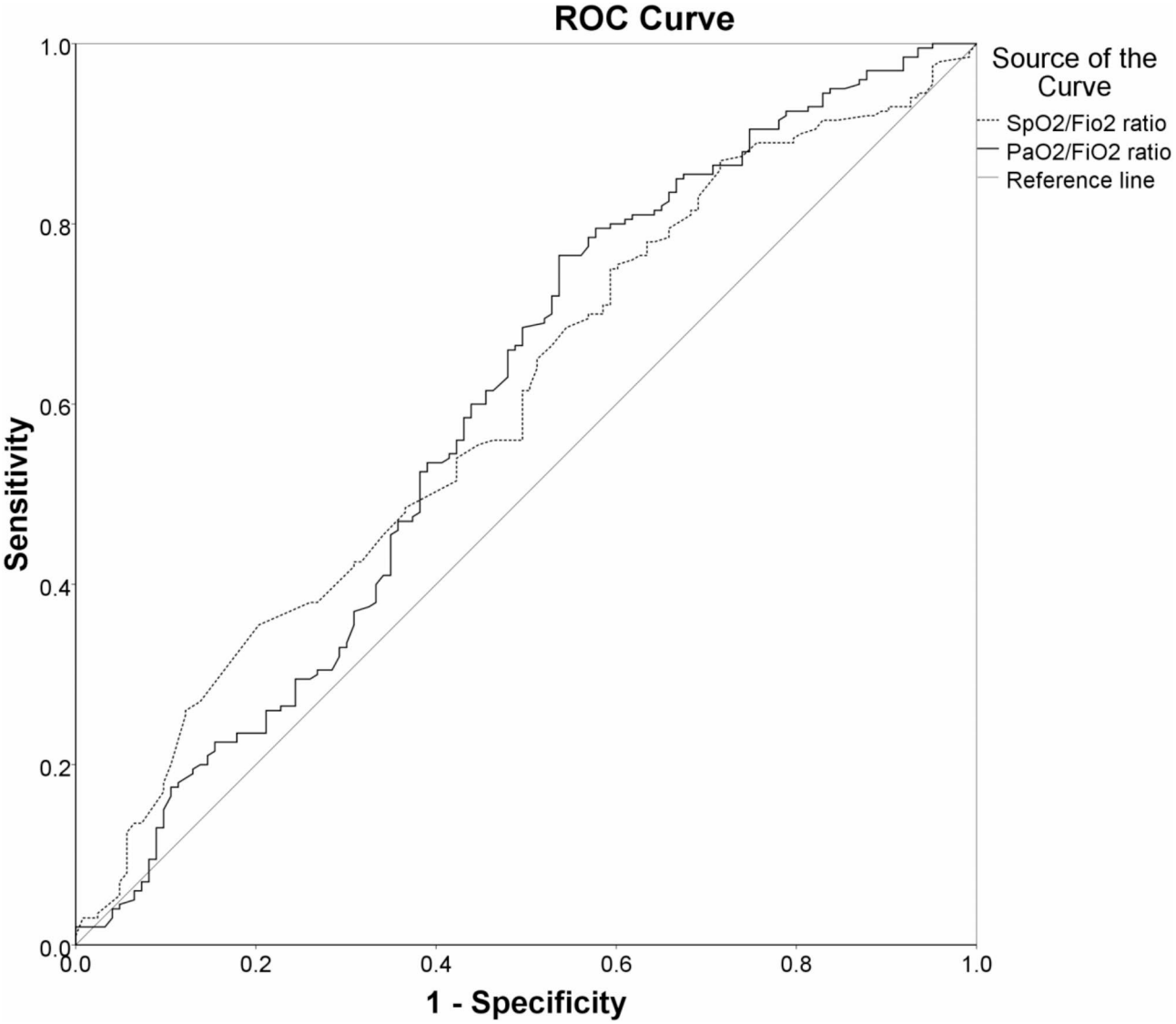

Fig. 3. Overall predictive performance of the SpO_2/FiO_2 and PaO_2/FiO_2 ratios for hospital mortality in ARDS patients. The SpO_2/FiO_2 ratio (AUROC: 0.595 [95% CI: 0.531–0.658]; cut-off value ≥ 90.50; sensitivity: 35.3%; specificity: 79.7%; P_{AUROC}=0.004) and the PaO_2/FiO_2 ratio (AUROC: 0.595 [95% CI: 0.529–0.660]; cut-off value ≥ 45.40; sensitivity: 76.2%; specificity: 46.0%; P_{AUROC}=0.004) demonstrated poor discriminatory ability for hospital mortality. An inverse correlation was observed between these ratios and hospital mortality rates. ARDS, acute respiratory distress syndrome; AUROC, the area under the receiver operator characteristic curve; CI, confidence interval; PaO_2/FiO_2, the ratio of the arterial oxygen partial pressure to the fraction of inspiratory oxygen concentration; SpO_2/FiO_2, the ratio of peripheral oxygen saturation to the fraction of inspiratory oxygen concentration.

PaO_2/FiO_2 ratio observed in our patients (Table 3). NMBAs are not routinely recommended for ARDS patients due to insufficient evidence of their benefits and potential adverse effects. Previous studies have indicated that paralysis and muscle relaxants are risk factors for HAP and sepsis/septic shock[52,53]. In the present study, HAP and septic shock were common complications (Table 4), significantly contributing to the elevated mortality rate[4]. Overall, our higher hospital mortality rate than those reported in the VALID, ALIEN, and LUNG SAFE studies suggest significant regional differences in patients, pathogens, and clinical capacity to manage ARDS, particularly between LMICs and HICs.

Predictive scoring systems, such as the PaO_2/FiO_2 ratio, the SpO_2/FiO_2ratio, the APACHE II score, and the SOFA score, are used to assess disease severity and predict outcomes, typically mortality, for critically ill ICU patients[2,8,15,20,54]. These measurements standardize research, improve treatment decisions, and evaluate patient care quality across ICUs. This study found that the PaO_2/FiO_2 ratio demonstrated poor discriminatory ability for hospital mortality (Fig. 3and Table S7 in Additional file 1), highlighting ongoing debates about its reliability[12–14,55–61]. A Chinese study showed excellent discrimination (AUROC: 0.865, 95% CI: 0.748–0.941) for predicting mortality in COVID-19 ICU patients[14], while an Italian study found poor discrimination

Factors	Univariable logistic regression analyses				Multivariable logistic regression analyses			
	OR	95% CI for OR		p-value	AOR	95% CI for AOR		p-value
		Lower	Upper			Lower	Upper	
SOFA score	1.168	1.093	1.250	< 0.001	1.132	0.985	1.301	0.081
SOFA score of ≥ 10[a]	2.692	1.709	4.242	< 0.001	3.398	1.300	8.880	0.013
APACHE II score	1.109	1.070	1.149	< 0.001	1.152	1.064	1.248	< 0.001
APACHE II score of ≥ 20[a]	3.612	2.230	5.851	< 0.001	4.433	1.663	11.818	0.003
SpO_2/FiO_2 ratio	0.994	0.989	0.999	0.019	0.985	0.973	0.996	0.010
PaO_2/FiO_2 ratio	0.993	0.989	0.997	< 0.001	0.989	0.980	0.997	0.009

Table 5. Association of severity scoring systems with hospital mortality. [a]To indicate the best cut-off value determined by analysing the receiver operator characteristic curve of severity scoring systems for predicting hospital mortality. AOR, adjusted odds ratio; APACHE II score, Acute Physiology and Chronic Health Evaluation II score; CI, confidence interval; OR, odds ratio; PaO_2/FiO_2 ratio, the ratio of the arterial oxygen partial pressure to the fraction of inspiratory oxygen concentration; SOFA score, Sequential Organ Failure Assessment score; SpO_2/FiO_2 ratio, the ratio of the peripheral oxygen saturation to the fraction of inspiratory oxygen concentration. See Tables S9 to S14 in Additional file 1 for additional information.

(AUROC: 0.688, 95% CI: 0.650–0.846)[13]. An earlier critique noted that while PaO_2 reflects oxygenation, its reliability decreases when expressed as a PaO_2/FiO_2ratio[12], leading to inconsistent data[13,14]. This study also found the PaO_2/FiO_2ratio inversely associated with hospital mortality, aligning with previous findings that mortality rates increase with worsening hypoxemia[2,8,54]. For instance, a multicentre study of 3022 ARDS patients reported mortality rates of 34.9% (249/714) for mild ARDS ($200 < PaO_2/FiO_2 \leq 300$ mmHg), 40.3% (446/1106) for moderate ARDS ($100 < PaO_2/FiO_2 \leq 200$ mmHg), and 46.1% (257/557) for severe ARDS ($PaO_2/FiO_2 \leq 100$ mmHg)[2]. Over the past decade, the SpO_2/FiO_2 ratio has increasingly replaced the PaO_2/FiO_2ratio for measuring hypoxemia[62–65], especially in resource-limited settings. A previous study used a nonlinear technique to estimate PaO_2/FiO_2 from SpO_2/FiO_2, outperforming others[64]. This study also found a strong correlation between SpO_2/FiO_2 and PaO_2/FiO_2 (Rs = 0.668, $p < 0.001$; detailed in Table S15 as shown in Additional file 1), and the SpO_2/FiO_2 ratio was identified as an independent predictor of hospital mortality (Table 5 and Table S13 in Additional file 1). The "New Global Definition" now includes $SpO_2/FiO_2$for oxygenation assessment[10]. However, this study found that SpO_2/FiO_2 exhibited poor discriminatory ability for hospital mortality (Fig. 3and Table S7 in Additional file 1), possibly due to measurement inaccuracies, especially in patients with darker skin, shock, or poor distal perfusion[66]. These findings suggest the need for further studies to focus on newer scoring systems to improve the accuracy of predicting outcomes for ARDS patients.

ARDS has a high mortality rate of around 40.1%[2].Several factors predict mortality, including illness severity scores. For instance, ARDS patients with higher APACHE III scores face an increased risk of death[67]. Similarly, a higher SOFA score correlates with worse outcomes[68]. However, this study found that both APACHE II and SOFA scores had poor discriminatory ability in predicting hospital mortality (Fig. 2, Table S7 in Additional file 1). Accurate data collection is challenging due to difficulties in determining whether deaths are directly due to ARDS or comorbidities such as cancer or organ dysfunction. The APACHE scoring system, used to predict mortality in ICU patients, has four versions (APACHE I-IV). Despite APACHE IV being the latest, some centres still use older versions such as APACHE II. Previous studies showed the APACHE II score had good prognostic value in acutely ill or surgical patients but was less effective in differentiating between sterile and infected necrotizing pancreatitis and predicting acute pancreatitis severity at 24 h[15–17]. This study also demonstrated that APACHE II was independently associated with hospital mortality (Table 5 and Tables S11 and S12) but exhibited poor discriminatory ability in predicting hospital mortality (Fig. 2, Table S7 in Additional file 1). The SOFA score, initially designed to assess organ dysfunction severity in sepsis patients, is now used to predict mortality in those with organ failure from other causes, including ARDS[2,18,69,70]. A retrospective study using data from various databases found the SOFA score had poor predictive ability for hospital mortality in ARDS patients, with AUROC values of 0.610, 0.620, and 0.650 for different cohorts[71]. This study confirmed the SOFA score's poor discriminatory ability in predicting hospital mortality (Fig. 2, Table S7 in Additional file 1) and found it was not significantly more accurate than the APACHE II score (Table S8 in Additional file 1). While the SOFA score was significantly associated with hospital mortality (Table 5, Table S9 in Additional file 1), only a score of ≥ 10 was an independent predictor of deaths in the hospital (Table 5, Table S9 in Additional file 1). Overall, the study highlights the importance of the APACHE II score and the SpO_2/FiO_2 and PaO_2/FiO_2 ratios as independent predictors of hospital mortality. It also suggests that the SOFA score may be significant at higher thresholds. However, the ability of these grading systems to predict hospital mortality is somewhat limited (Figs. 2 and 3 and Table S7 in Additional file 1). Notably, the SOFA score did not significantly outperform the APACHE II score (Table S8 in Additional file 1). These findings underscore the need for new scoring systems to enhance the accuracy of outcome predictions for ARDS patients.

The present study has certain limitations. *Firstly*, its retrospective design restricted the availability of data for many variables (Table S16 in Additional file 1). For instance, we only had information on CCI for 148 patients.

Secondly, the study was conducted at a single centre in Hanoi, Vietnam, focusing on a highly selected population of cases transferred from local hospitals to the highest-level public sector hospitals in Vietnam. As a result, the number of patients with ARDS is likely to be significantly higher. *Lastly*, not all patients with ARDS from local hospitals were referred to the participating central hospital; only those with deteriorating conditions were transferred. This implicit selection bias and incomplete patient inclusion in the study database could potentially skew the mortality rate, resulting in an overestimation of fatalities.

Conclusion

This study investigated a selected cohort of ARDS patients with a high mortality rate admitted to a central hospital in Vietnam. Our findings highlight the importance of the APACHE II score and the SpO_2/FiO_2 and PaO_2/FiO_2 ratios as independent predictors of hospital mortality in this patient population. Although the SOFA score showed potential significance at higher thresholds (≥ 10) for predicting hospital mortality, its effect size was less than that of the APACHE II score and the SpO_2/FiO_2 and PaO_2/FiO_2 ratios. Additionally, the discrimination ability of these scores and ratios for hospital mortality was poor, with the SOFA score not demonstrating significantly greater accuracy than the APACHE II score. These findings suggest the need for further studies to focus on newer scoring systems to improve the accuracy of predicting outcomes for ARDS patients.

Data availability

All data generated or analysed during this study are included in this published article (and its Supplementary Information files).

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Author contributions

CXD and TQD contributed to the design of the work, and interpretation of data for the work and revised the draft critically for important intellectual content; CQL contributed to the conception, design of the work, acquisition, analysis, and interpretation of data for the work, wrote the first draft of the work and revised the draft critically for important intellectual content; TM, MHN, and DTP contributed to the design of the work, analysis, and interpretation of data for the work; QTP, TTV, HTT, HHN, CBN, DQK, and HDD contributed to the acquisition and interpretation of data for the work; TAN, TTP, GTHB, CVB, QHN, THT, TCN, KHV, and LTV contributed to the interpretation of data for the work; NTP, PTHN, and CDN contributed to the analysis and interpretation of data for the work; AND, CVN, and BGN contributed to the interpretation of data for the work and revised the draft critically for important intellectual content. SND contributed to the conception, design of the work, and interpretation of data for the work and revised the draft critically for important intellectual content. All authors reviewed and edited the work and approved its final version. CQL is responsible for the overall content as the guarantor.

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