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ORIGINAL RESEARCH

Predictors of non-invasive ventilation failure in adult patients with cardiac dysfunction presenting with community-acquired pneumonia: an Egyptian multicenter prospective study

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Abstract

Non-invasive ventilation (NIV) might be successful if carefully selected in adult patients with cardiac dysfunction presenting with community-acquired pneumonia. The main objective of this study was to identify the early predictors of NIV failure. Adult patients with left ventricle ejection fraction (LV EF) <50% admitted to the intensive care unit (ICU) with community-acquired pneumonia and acute respiratory failure were enrolled in this multicenter prospective study after obtaining informed consents (study registrationID: ISRCTN14641518). Non-invasive ventilation failure was defined as the requirement of intubation after initiation of NIV. All patients were assessed using the Acute Physiology and Chronic Health Evaluation II (APACHE II) and sequential organ failure assessment (SOFA) scores at admission, while their Heart rate Acidosis Consciousness Oxygenation and Respiratory rate (HACOR) and lung ultrasound (LUS) scores in addition to blood lactate were assessed at NIV initiation and 12 and 24 hours later. A total of 177 patients were prospectively enrolled from February 2019 to July 2020. Of them, 53 (29.9%) had failed NIV. The mean age of the study cohort was 64.1 $\pm$ 12.6 years, with a male predominance (73.4%) and a mean LV EF of 36.4 $\pm$ 7.8%. Almost 55.9% of the studied patients had diabetes mellitus, 45.8% had chronic systemic hypertension, 73.4% had ischemic heart disease, 20.3% had chronic kidney disease, and 9.6% had liver cirrhosis. No significant differences were observed between the NIV success and NIV failure groups regarding underlying morbidities or inflammatory markers. Patients who failed NIV were significantly older and had higher mean SOFA and APACHE II scores than those with successful NIV. We also found that NIV failure was associated with longer ICU stay ($p < 0.001$), higher SOFA scores at 48 hours ($p < 0.001$) and higher mortality ($p < 0.001$) compared with the NIV success group. In addition, SOFA (Odds Ratio (OR): 4.52, 95% Confidence Interval (CI): 2.59–7.88, $p < 0.001$), HACOR (OR: 2.01, 95% CI: 0.97–4.18, $p = 0.036$) and LUS (OR: 1.33, 95% CI: 1.014–1.106, $p = 0.027$) scores and blood lactate levels (OR: 9.35, 95% CI: 5.32–43.26, $p < 0.001$) were independent factors for NIV failure. High initial HACOR and SOFA scores, persistent hyperlactatemia and non-decrementing LUS score were associated with early NIV failure in patients with cardiac dysfunction presenting with community-acquired pneumonia, and could be used as clinical and paraclinical variables for early decision making regarding invasive ventilation.

Keywords

Non-invasive ventilation; Pneumonia; Lung ultrasound (LUS); Lactate; HACOR score; APACHE II; SOFA score; Heart failure

1. Background

Community-acquired pneumonia (CAP) can lead to acute deterioration of pre-existing heart disease and trigger new acute cardiac complications [1, 2]. The associated cardiac manifestations may relate to endothelial dysfunction, coronary plaques instability, changes in peripheral vascular resistance and blood coagulability [2]. Pulmonary edema and pneumonia are the most frequent causes of respiratory distress and acute respiratory failure in adult patients with systolic cardiac dysfunction [3]. Acute respiratory failure may occur due to excess alveoli

and interstitial fluid accumulation, resulting in a shunt effect. During cardiogenic shock, the resulting tissue hypoperfusion leads to lactic acidosis, and hypoperfusion causes pulmonary dead space ventilation, which increases ventilation-perfusion mismatching with more hypoxemia and hypercapnia [3–5]. Non-invasive ventilation (NIV) is a ventilatory support modality delivering positive pressure to conscious patients without endotracheal tube insertion. The main applications of NIV consist of continuous positive airway pressure (CPAP) by maintaining a positive end-expiratory pressure (PEEP) and bilevel positive pressure ventilation (BiPAP) *via* PEEP and inspiratory pressure support (IPAP). Positive pressure ventilation prevents alveoli's collapse and keeps them open, resulting in improved gas exchange and decreased work of breathing. The cardiovascular effects of positive pressure ventilation include decreased venous return, decreased left ventricular afterload, increased pulmonary vascular resistance, and increased right ventricle afterload [6–8].

NIV is widely used in patients with cardiac dysfunctions presenting with respiratory failure to decrease the work of breathing, improve oxygenation and avoid endotracheal intubation with sedation and concomitant hemodynamics effects [3]. The use of NIV in patients with acute hypoxemic respiratory failure related to pneumonia is associated with higher risks compared with its use in other diagnoses like chronic obstructive pulmonary disease or cardiogenic pulmonary edema [9–11]. In addition, NIV is associated with many challenges, including patient-ventilator asynchrony, air leaks and titration of positive end-expiratory pressure and inspiratory pressure support. Other challenges in cardiac patients with pneumonia include respiratory secretions and the underlying pathologic processes of sepsis, which may precipitate hemodynamic compromise and cardiac events.

Previous studies reported that NIV might be more successful in a small subset of carefully selected patients [10–13], but data on the accurate selection of patients are limited. Thus, the objective of this study was to prospectively identify the early predictors of NIV failure in adult patients with cardiac systolic dysfunction presenting with CAP.

2. Methods

2.1 Study design and patient enrollment

This multicenter prospective observational study was performed at the critical care units of 5 different hospitals.

The SPICE framework, which builds upon the PICO acronym (Population, Intervention, Comparison and Outcomes), was implemented in a step-by-step approach to formulate practice questions to obtain evidence for this present study [14].

The framework consists of five components:

1. Setting: prospective study enrolling adult patients with cardiac systolic dysfunction admitted to ICU with acute respiratory failure.
2. Perspective: patients with heart failure admitted to the ICU due to CAP with hypoxemic respiratory failure.
3. Intervention: non-invasive ventilatory support.
4. Comparison: clinical and paraclinical assessments were performed to compare patients who had successful NIV with those who failed NIV.
5. Evaluation: outcomes included hospital mortality rate and length of ICU stay.

The consort flow diagram of this study is shown in Fig. 1. Initially, 310 patients were assessed for eligibility, of whom 46 were excluded due to do-not-intubate orders, presence of chronic obstructive pulmonary disease, requirement for emergency intubation, severe acute respiratory distress syndrome (ARDS), *i.e.*, the ratio of arterial oxygen partial pressure (PaO_2) to fractional inspired oxygen (FiO_2); P/F ratio$<$ 150, and NIV intolerance. NIV intolerance was defined as a patient's refusal of NIV because of discomfort. After excluding 87 patients who refused to participate, a total of 177 patients were enrolled and informed consents were obtained from recruited patients or their kins. As there was no standard method to predict NIV failure, we could not obtain the known sensitivity and specificity. Based on clinical experience, we estimated that the risk scale for NIV failure achieved a sensitivity and specificity of 80% each. Comparatively, the average prevalence of NIV failure was reported to range between 50–60% in previous studies [15–20]. Based on an α = 0.05 and maximum marginal error of estimate =5%, a minimal sample size of 154 cases was required for this study.

2.2 Patients management and studied variables

The decision to initiate NIV was made by the attending physicians based on the following considerations: clinical presentation of respiratory distress at rest, partial pressure of arterial oxygen (PaO_2) $<$60 mmHg or a PaO_2/fraction of inspired oxygen (FiO_2) ratio ranging between 150–300 with supplemental oxygen. The recruited patients were placed in a semi-recumbent position, and their positive-end expiratory pressure was maintained at 4–8 cmH_2O. Inspiratory pressure was initially set at 10 cmH_2O and incremented by 2 cmH_2O to achieve optimal control of dyspnea and patient's tolerance. If a patient could not tolerate it, the inspiratory pressure was decreased to 6–8 cmH_2O, if needed. The fractional oxygen concentration was set to achieve a peripheral oxygen saturation of $>$92%. NIV was used intermittently until the patient was completely weaned from it.

In this study, NIV failure was defined as the requirement of intubation and invasive mechanical ventilation (MV) within the first 48 hours of NIV intervention (early NIV failure), based on the following criteria: presence of respiratory or cardiac arrest, failure to maintain a PaO_2/FiO_2 $>$100, development of conditions necessitating intubation to protect the airway (*i.e.*, impaired consciousness or seizures) or to manage copious tracheal secretions, inability to correct dyspnea, lack of improvement of signs of respiratory muscle fatigue, and hemodynamic instability without response to fluids and vasoactive agents [11, 21, 22].

Next, the patients were divided into an NIV success group and an NIV failure group and the following clinical and paraclinical variables were recorded and assessed:

I. Demographic profiles.

II. Vital signs and need for vasopressors.

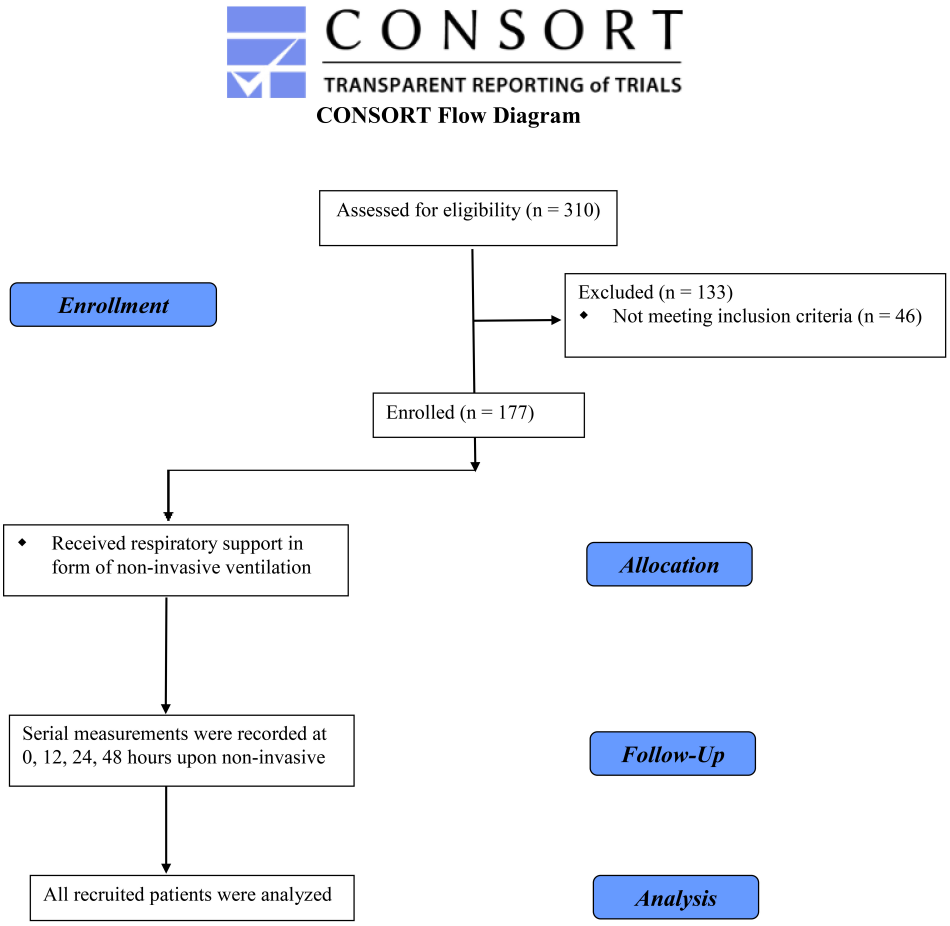

FIGURE 1. Consort flow diagram showing the recruitment and follow-up of this study.

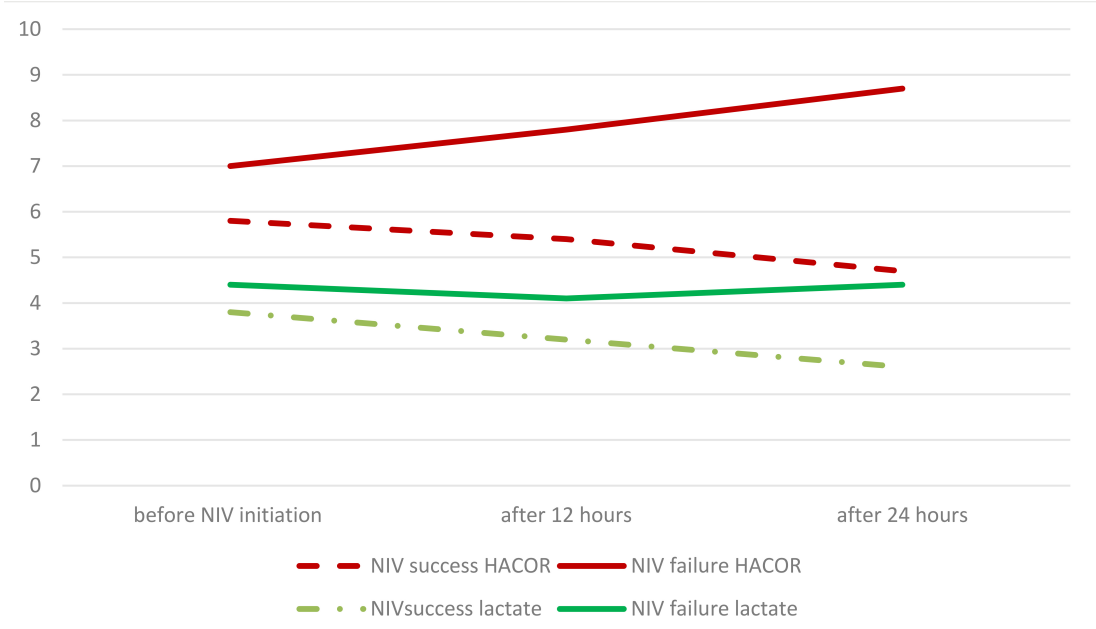

FIGURE 2. Trends of HACOR and blood lactate in the NIV success and failure groups. The solid red line represents the up-trending of the HACOR score in the NIV failure group, while the dashed red line represents the down-trending of HACOR in the NIV success group. The dashed dot green line represents the decrease of blood lactate in the NIV success group, while the solid green line represents persistently high blood lactate in the NIV failure group.
HACOR: Heart rate Acidosis Consciousness Oxygenation and Respiratory rate; NIV: Non-Invasive Ventilation.

III. Laboratory investigations, including arterial blood gases, complete blood count, INR, serum creatinine, C-reactive protein, serum bilirubin, procalcitonin, serum albumin, B-type natriuretic peptide, arterial blood lactate and troponin. Blood lactate was measured at NIV initiation, then 12 and 24 hours later.

IV. The patients' condition was scored using the following: Sequential Organ Failure Assessment (SOFA), acute physiology and chronic health evaluation II (APACHE II) scores, Heart rate, Acidosis (pH), Consciousness (GCS), Oxygenation and Respiratory rate (HACOR) score and Lung ultrasound (LUS) score.

V. The study outcomes assessed included NIV failure, hospital mortality, development of acute kidney injury, need for dialysis and length of ICU stay.

A newly proposed scoring method that relied primarily on 5 variables; Heart rate, Acidosis (pH), Consciousness (GCS), Oxygenation and Respiratory rate (HACOR) has been described by Duan and his colleagues [23, 24]. This HACOR score was recorded at NIV initiation, then after 1, 12 and 24 hours if it was still used.

LUS was determined using a 2–5 MHz convex probe. The patient was positioned in a supine and lateral decubitus position, and each lung was divided into 3 zones and examined anteriorly and posteriorly to assess the degree of lung aeration for a total of 12 lung zones. The scoring was performed as follows:

(1) Normal aeration: the presence of lung sliding with A-lines or less than two isolated B lines (score 0)

(2) Moderate loss of lung aeration: multiple B lines (score 1)

(3) Severe loss of lung aeration: multiple fused B lines (score 2)

(4) Lung consolidation: the presence of dynamic air bronchograms and tissue patterns (score 3).

The final score (range, 0 to 36) represents the sum of the values, from 0 to 3, assigned to the LUS patterns visualized in each of the 12 examined regions [25, 26]. LUS was recorded at NIV initiation, then 12 and 24 hours later.

2.3 Statistical analysis

Statistical analysis was performed using the statistical package for the Social Sciences (SPSS) version 26 (IBM Corp., Armonk, NY, USA). The data are reported as the mean and standard deviation (SD). Normally distributed continuous variables were analyzed using the unpaired Student's *t*-test. Non-normally distributed continuous variables were analyzed using the Mann-Whitney U test. Categorical variables were analyzed using the Chi-squared test or Fisher's exact test. The ability to predict NIV failure was determined using the area under the receiver operating characteristic curve (AUROC). A p-value < 0.05 was considered statistically significant.

Univariate analysis was performed to identify variables associated with NIV failure, following which variables of $p < 0.2$ were entered in a stepwise multivariate logistic regression analysis to identify independent risk factors associated with NIV failure. The probability of stepwise was 0.05 for entry and 0.1 for removal, based on which a regression model was obtained. We also evaluated the final model for the goodness of fit using the Hosmer-Lemeshow test ($p > 0.05$).

3. Results

3.1 Demographic and clinical variables of the studied patients

The mean age of the study cohort was 64.1 ± 12.6 years, had a male predominance (73.4%) and a mean left ventricle EF of 36.4 ± 7.8%. The patients with NIV failure were significantly older than those with successful NIV (67.1 ± 13.3 versus 62.7 ± 12.2, $p = 0.034$), while no significant differences were observed regarding sex, smoking, diabetes mellitus, chronic kidney disease (CKD), liver cirrhosis, ischemic disease, LV EF and cardiac and inflammatory laboratory markers between both groups. The initial blood lactate at NIV initiation was 3.8 ± 0.5 *vs.* 4.4 ± 0.3 ($p < 0.001$), and lactate after 12 hours was 3.2 ± 0.6 *vs.* 4.1 ± 0.4 ($p < 0.001$), while lactate after 24 hours was 2.6 ± 0.6 *vs.* 4.4 ± 0.4 ($p < 0.001$) in the NIV success and NIV failure groups, respectively. Intravenous vasopressor and inotropic drips were used in 24.2% *vs.* 54.5% ($p < 0.001$) of patients in the NIV success and NIV failure groups, respectively (Table 1).

3.2 Scoring and outcomes of patients

The patients who failed NIV were found to have higher APACHE II (17.5 ± 3.5 *vs.* 11.3 ± 3.7, $p < 0.001$), initial SOFA (8.5 ± 1.5 *vs.* 5.5 ± 2.1, $p < 0.001$) and follow up SOFA scores after 48 hours of NIV initiation (8.9 ± 1.8 *vs.* 5.3 ± 1.9, $p < 0.001$) than those with successful NIV. HACOR scores were calculated at 4 points, and the results showed that patients who failed NIV had significantly and persistently higher HACOR scores than those with successful NIV. The HACOR score for the NIV success group versus NIV failure group was 5.8 ± 1.1 *vs.* 7.0 ± 1.3 ($p < 0.001$) at T0, 5.6 ± 1.3 *vs.* 7.3 ± 1.9 ($p < 0.001$) at TI, 5.4 ± 1.7 *vs.* 7.8 ± 2.7 ($p < 0.001$) at T12, and 4.7 ± 1.5 *vs.* 8.7 ± 1.6 ($p < 0.001$) at T24, respectively. The LUS score for the NIV success group versus NIV failure group was 15.5 ± 4.0 *vs.* 18.9 ± 3.9 ($p < 0.001$) at T0, 15.3 ± 4.3 *vs.* 19.1 ± 4.2 ($p < 0.001$) at T12, and 14.4 ± 4.3 *vs.* 20.1 ± 4.4 ($p < 0.001$) at T24, respectively. The incidence of acute kidney injury, the need for dialysis, and hospital mortality were lower in the NIV success group compared with the NIV failure group (57.26% *vs.* 88.7% ($p = 0.02$), 19.35% *vs.* 79.25% ($p < 0.001$), and 1.6% *vs.* 66% ($p < 0.001$), respectively) (Table 2, Fig. 2).

3.3 Predictors of NIV failure

Multivariate regression analysis was performed to identify the potential predictors of early NIV failure. The results showed that NIV failure was independently associated with SOFA (OR: 4.52, 95% CI: 2.59–7.88, $p < 0.001$), HACOR score (OR: 2.01, 95% CI: 0.97–4.18, $p = 0.036$), LUS score (OR: 1.33, 95% CI: 1.014–1.106, $p = 0.027$) and blood lactate (OR: 9.35, 95% CI: 5.32–43.26, $p < 0.001$). Although the APACHE II score was significantly different in the univariate analysis, it was removed from the multivariate regression model due to

TABLE 1. Admission variables of the studied patients.

Variables	All patients (n = 177)	NIV success (124, 70.1%)	NIV failure (53, 29.9%)	*p* value
Age (yrs)	64.1 ± 12.6	62.7 ± 12.2	67.1 ± 13.3	0.034
Sex, male (n, %)	130 (73.4)	92 (74.2)	38 (71.7)	0.8
Smoking (n, %)	99 (55.9)	67 (54)	32 (60.4)	0.1
Diabetes (n, %)	99 (55.9)	62 (50)	37 (69.8)	0.06
Hypertension (n, %)	81 (45.8)	58 (46.8)	23 (43.4)	0.3
Chronic kidney disease (n, %)	36 (20.3)	24 (19.4)	12 (22.6)	0.15
Liver cirrhosis (n, %)	17 (9.6)	11 (8.9)	6 (11.3)	0.4
Ischemic heart disease (n, %)	130 (73.4)	89 (71.8)	41 (77.4)	0.2
Left ventricle EF (%)	36.4 ± 7.8	38.4 ± 12.6	34.6 ± 9.4	0.06
MAP (mmHg)	84 ± 22	86 ± 18	81 ± 21	0.32
Heart rate (beats/min)	115 ± 14	107 ± 21	121 ± 16	0.03
Respiratory rate (breath/min)	29 ± 4	28 ± 3	29 ± 6	0.1
Temperature (°C)	37.5 ± 0.46	37.4 ± 0.80	37.6 ± 0.70	0.8
Hemoglobin (g/dL)	12.1 ± 2.7	12.5 ± 2.3	11.9 ± 3.1	0.5
White blood cells (× 10^3/mL)	15.6 ± 2.9	14.2 ± 2.7	16.4 ± 3.4	0.4
Platelets (× 10^3/mL)	204 ± 36	214 ± 67	187 ± 48	0.2
INR	1.1 ± 0.47	1.1 ± 0.40	1.08 ± 0.60	0.8
Serum creatinine (mg/dL)	1.3 ± 0.78	1.3 ± 0.90	1.4 ± 0.07	0.7
Serum bilirubin (mg/dL)	1.4 ± 0.7	1.4 ± 0.36	1.5 ± 0.70	0.6
Albumin level (mg/dL)	4.1 ± 0.84	4.2 ± 0.90	3.9 ± 1.10	0.2
C-reactive protein (mg/L)	153 ± 49	162 ± 68	148 ± 51	0.3
Procalcitonin (ng/mL)	11.3 ± 2.4	10.48 ± 3.4	11.61 ± 2.9	0.3
Troponin I	405 ± 59	426 ± 86	392 ± 73	0.6
Pro-BNP (pg/mL)	3865 ± 819	3278 ± 1090	4198 ± 789	0.07
pH	7.23 ± 0.04	7.24 ± 0.06	7.22 ± 0.03	0.03
$PaCO_2$ (mmHg)	81 ± 12	82 ± 16	78 ± 14	0.21
PaO_2/FiO_2	189 ± 69	197 ± 98	182 ± 74	0.38
Lactate at T0 (mmol/L)	4.0 ± 0.5	3.8 ± 0.5	4.4 ± 0.3	<0.001
Lactate at T12 (mmol/L)	3.1 ± 0.4	3.2 ± 0.6	4.1 ± 0.4	<0.001
Lactate at T24 (mmol/L)	3.5 ± 0.7	2.6 ± 0.6	4.4 ± 0.4	<0.001
Vasopressors	72 (40.7%)	30 (24.2%)	42 (54.5%)	<0.001

Data are presented as mean (±SD) or N (%).
MAP: Mean arterial blood pressure; EF: ejection fraction; INR: international normalized ratio; BNP: B-type natriuretic peptide; $PaCO_2$: arterial carbon dioxide partial pressure; PaO_2: arterial oxygen partial pressure; FiO_2: fraction of inspired oxygen; NIV: Non-invasive ventilation.

TABLE 2. Scoring and outcomes of the studied patients.

Variables	All patients	NIV success	NIV failure	*p* value
APACHE II	13.1 ± 4.6	11.3 ± 3.7	17.5 ± 3.5	<0.001
SOFA at admission	6.4 ± 2.3	5.5 ± 2.1	8.5 ± 1.5	<0.001
SOFA at 48 h	6.7 ± 2.6	4.8 ± 1.9	8.9 ± 1.8	<0.001
HACOR T0	6.2 ± 1.2	5.8 ± 1.1	7.0 ± 1.3	<0.001
HACOR T1	6.1 ± 1.7	5.6 ± 1.3	7.3 ± 1.9	<0.001
HACOR T12	6.1 ± 2.3	5.4 ± 1.7	7.8 ± 2.7	<0.001
HACOR T24	6.1 ± 1.92	4.7 ± 1.5	8.7 ± 1.6	<0.001
LUS T0	16.6 ± 4.2	15.5 ± 4.0	18.9 ± 3.9	<0.001
LUS T12	16.5 ± 4.6	15.3 ± 4.3	19.1 ± 4.2	<0.001
LUS T24	16.1 ± 5.1	14.4 ± 4.3	20.1 ± 4.4	<0.001
NIV duration (h)	31.8 ± 9.0	33.0 ± 8.6	29.0 ± 9.5	0.007
ICU days	9.6 ± 4.3	8.5 ± 3.3	12.2 ± 5.2	<0.001
AKI (n, %)	118 (66.7)	71 (57.26)	47 (88.7)	0.020
Need for dialysis (n, %)	66 (37.28)	24 (19.35)	42 (79.25)	<0.001
Hospital mortality (n, %)	37 (20.9%)	2 (1.6%)	35 (66.0%)	<0.001

APACHE II: Acute Physiology and Chronic Health Evaluation II; SOFA: sequential organ failure assessment; HACOR: Heart rate Acidosis Consciousness Oxygenation and Respiratory rate; LUS: Lung Ultrasound; NIV: Non-Invasive Ventilation; AKI: Acute Kidney Injury; ICU: intensive care unit.

collinearity with the HACOR score (Table 3).

An admission SOFA score at a cutoff of 7 demonstrated a 90.6% sensitivity and 81.5% specificity (AUROC: 0.882, $p < 0.001$) for predicting NIV failure at NIV initiation. Further, a blood lactate cutoff of 4 mmol/L at T0 demonstrated a sensitivity of 94.3% and specificity of 56.5% (AUROC: 0.856, $p < 0.001$) for predicting NIV failure at NIV initiation, while that for initial HACOR score (cutoff, 7) demonstrated a sensitivity of 77.4% and specificity of 66.9% (AUROC: 0.757, $p < 0.001$), HACOR score at T1 (cutoff, 8) demonstrated a sensitivity of 71.7% and specificity of 76.6% (AUROC: 0.791, $p < 0.001$), initial LUS score at T0 (cutoff, 18) demonstrated a sensitivity of 62.3% and specificity of 61.3% (AUROC: 0.728, $p < 0.001$), and APACHE II (cutoff, 16) demonstrated a sensitivity of 84.9% and a specificity of 83.1% (AUROC: 0.879, $p < 0.001$) (Table 4, Fig. 3).

A HACOR score at a cutoff of 7 demonstrated a sensitivity of 73.6% and specificity of 72.6% (AUROC: 0.796, $p < 0.001$) for predicting NIV failure after 12 hours of NIV initiation, while that for LUS score at T12 (cutoff, 18) showed a 64.2% sensitivity and 59.7% specificity (AUROC: 0.727), blood lactate at T12 (cutoff, 4 mmol/L) showed a 92.5% sensitivity and 56% specificity (AUROC: 0.815, $p < 0.001$) for predicting NIV failure after 12 hours of NIV initiation (Table 4, Fig. 4).

In regard to predicting NIV failure after 24 hours of NIV initiation, a HACOR score at a cutoff of 7 demonstrated a sensitivity of 87.2% and a specificity of 79.3% (AUROC: 0.94, $p < 0.001$), LUS score at T24 (cutoff, 18) demonstrated a sensitivity of 66% and a specificity of 74.2% (AUROC: 0.79, $p < 0.001$), and blood lactate at T24 (cutoff, 4 mmol/L) demonstrated a sensitivity of 73.4% and a specificity of 73.4% (AUROC: 0.954, $p < 0.001$) (Table 4, Fig. 5).

TABLE 3. Multivariate analysis of predictors for NIV failure.

Variables	Odds ratio	95% CI	*p* value
HACOR	2.009	0.966–4.177	0.036
Lactate	9.353	5.321–43.262	<0.001
LUS score	1.331	1.014–1.106	0.027
SOFA	4.520	2.593–7.877	<0.001

HACOR: Heart rate Acidosis Consciousness Oxygenation and Respiratory rate; LUS: Lung Ultrasound; SOFA: sequential organ failure assessment; CI: Confidence interval.

4. Discussion

The main findings of this study were that NIV failure in systolic dysfunction patients presenting with CAP was associated with longer ICU stay, an increasing trend of SOFA score after 48 hours, and higher hospital mortality than patients who had successful NIV. Further, NIV failure was independently associated with SOFA (OR: 4.52, 95% CI: 2.59–7.88, $p <$

TABLE 4. Details of receiver operator characteristic curves in predicting NIV failure.

Variables	AUROC	*p* value	Cutoff	sensitivity	specificity	PPV	NPV	Accuracy
At NIV initiation								
HACOR T0	0.757	<0.001	7	77.4%	66.9%	50.0%	87.4%	70.1%
HACOR T1	0.791	<0.001	8	71.7%	76.6%	56.7%	86.4%	75.1%
LUS T0	0.728	<0.001	18	62.3%	61.3%	40.7%	79.2%	61.6%
Lactate T0	0.856	<0.001	4.0	94.3%	56.5%	48.1%	95.9%	67.8%
APACHE II	0.879	<0.001	16	84.9%	83.1%	68.2%	92.8%	83.6%
SOFA	0.882	<0.001	7	90.6%	81.5%	67.6%	95.3%	84.2%
At 12 h (T12)								
HACOR T12	0.796	<0.001	7	73.6%	72.6%	53.4%	86.5%	72.9%
LUS T12	0.727	<0.001	18	64.2%	59.7%	39.3%	79.6%	61.0%
Lactate T12	0.815	<0.001	4.0	92.5%	56.5%	47.6%	94.6%	67.2%
At 24 h (T24)								
HACOR T24	0.940	<0.001	7	87.2%	79.3%	63.1%	93.9%	81.6%
LUS T24	0.790	<0.001	18	66.0%	74.2%	49.3%	83.6%	71.8%
Lactate T24	0.954	<0.001	4.0	96.2%	73.4%	60.7%	97.8%	80.2%

APACHE II: Acute Physiology and Chronic Health Evaluation II; SOFA: sequential organ failure assessment; HACOR: Heart rate Acidosis Consciousness Oxygenation and Respiratory rate; LUS: Lung Ultrasound; AUROC: Area Under Receiver Operator Characteristic; PPV: Positive Predictive Value; NPV: negative predictive value.

0.001), HACOR score (OR: 2.01, 95% CI: 0.97–4.18, p = 0.036), LUS score (OR: 1.33, 95% CI: 1.014–1.106, p = 0.027) and blood lactate level (OR: 9.35 ,95% CI: 5.32–43.26, $p <$ 0.001).

Our results showed a lower hospital mortality rate in the NIV success group compared with the NIV failure group (1.6% *vs.* 66%, $p < 0.001$). Rodríguez *et al.* [27] conducted a large prospective study for NIV in critically ill patients and found that the ICU mortality in the NIV success group was also lower than in the NIV failure group (6.3% *vs.* 38.4%, $p <$ 0.001), with NIV failure identified as an independent predictor of mortality. The difference in mortality can be explained by the different study populations. In this present study, the patients were older, with a mean age of 64.1 ± 12.6 years, and had a greater left ventricle EF (36.4 ± 7.8%) compared with those in the study of Rodríguez *et al.* [27] (median age, 53 (41–64)), with only 12.3% of them having cardiac disease.

NIV is widely used in patients with systolic cardiac dysfunctions presenting with acute respiratory failure to decrease the work of breathing, improve oxygenation through recruitment of collapsed alveoli, decrease left ventricular pre-and-afterloads and avoid endotracheal intubation with sedation and possible concomitant hemodynamics effects [3]. The NIV success and failure groups showed no significant differences regarding cardiac systolic dysfunction, known coronary artery disease and admission cardiac biomarkers and inflammatory markers. Our main objective was to identify the early predictors of NIV failure to avoid delayed intubation, which was linked to mortality in many previous studies [28–33]. We could not determine the accurate number of cardiac complications during ICU stay due to the interplay between heart failure and sepsis. Corrales-Medina *et al.* [1] reported that cardiac complications occurred in more than one-quarter of hospitalized patients with CAP mainly in the first 7 days of stay and >50% of them occurred on the same day of CAP diagnosis. The presence of pneumonia exposes cardiac patients to risks of acute cardiac events due to cytokines-mediated systemic inflammatory response resulting in endothelial dysfunction, coronary plaques instability and changes in peripheral vascular resistance and blood coagulability [2]. Sepsis-induced tachycardia was shown to increase myocardial oxygen requirements and decrease coronary perfusion due to shortened diastole [34, 35]. Acute hypoxemia due to alveoli collapse can decrease myocardial oxygen supply and increase pulmonary pressure and right ventricle afterload [36, 37]. The proinflammatory and prothrombotic changes with pneumonia may result in coronary plaques instability and precipitating myocardial infarctions [2]. Moreover, sepsis-induced cardiomyopathy is a well-known complication resulting from endothelial dysfunction, mitochondrial oxidative stress, macro-and-microcirculatory changes, downregulation of beta-adrenoreceptors and apoptosis of cardiomyocytes [38, 39].

Duan *et al.* [23] proposed the HACOR score and reported

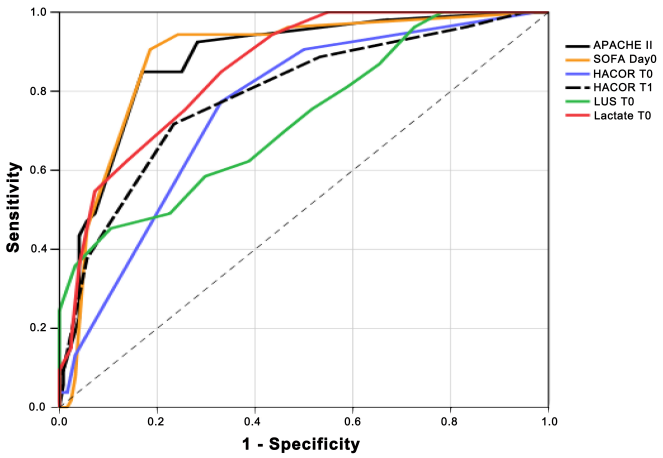

FIGURE 3. ROC curves to predict NIV failure at initiation. The blue curve represents the HACOR score at T0 (AUROC 0.757), the black interrupted curve represents HACOR T1 (AUROC 0.791), the red curve represents blood lactate (AUROC 0.856), the green curve represents LUS (AUROC 0.728), the continuous black curve represents APACHE II (AUROC 0.879), and the yellow curve represents SOFA score (AUROC 0.728).
APACHE II: Acute Physiology and Chronic Health Evaluation II; SOFA: sequential organ failure assessment; HACOR: Heart rate Acidosis Consciousness Oxygenation and Respiratory rate; LUS: Lung Ultrasound.

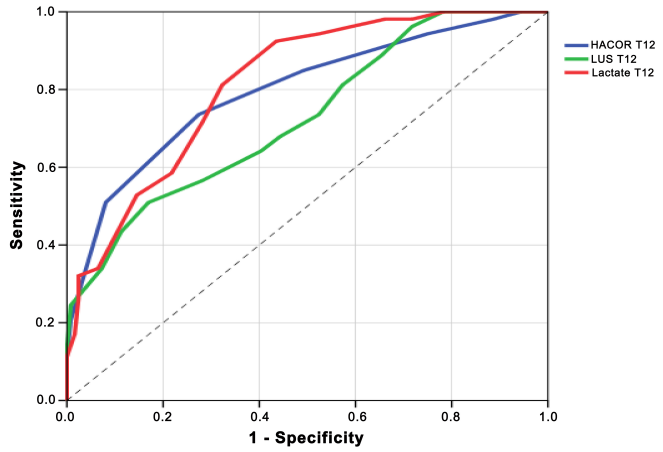

FIGURE 4. ROC curves to predict NIV failure after 12 hours of NIV initiation. The blue curve represents the HACOR score (AUROC 0.796), the red curve represents blood lactate (AUROC 0.815), and the green curve represents LUS (AUROC 0.727). HACOR: Heart rate Acidosis Consciousness Oxygenation and Respiratory rate; LUS: Lung Ultrasound.

that it was higher in the NIV failure group than in the NIV success and a cutoff value of 5 at T0 or T1 had good distinguishing power for NIV failure. Our results also showed that the HACOR score was significantly higher in the NIV failure group compared with the NIV success group and was an independent predictor of NIV failure. However, the performance of the HACOR score was lesser than that observed by Duan *et al.* [23]. In this present study, a HACOR score at a cutoff

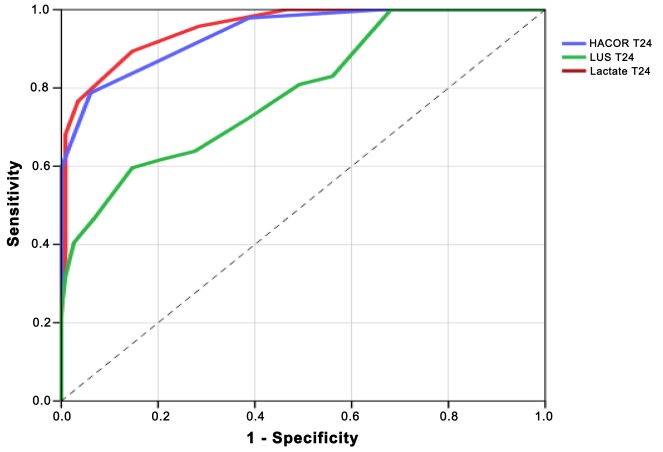

FIGURE 5. ROC curves to predict NIV failure after 24 hours of NIV initiation. The blue curve represents the HACOR score (AUROC 0.94), the red curve represents blood lactate (AUROC 0.954), and the green curve represents LUS (AUROC 0.790). HACOR: Heart rate Acidosis Consciousness Oxygenation and Respiratory rate; LUS: Lung Ultrasound.

value of 7 at T0 demonstrated good distinguishing power for NIV failure with an AUROC of 0.757, while a cutoff of 8 at T1 (AUROC, 0.791), 7 at T12 (AUROC, 0.796) and 7 at T24 (AUROC, 0.94) was shown to have good distinguishing power for NIV failure. We hypothesized that the difference in performance between the 2 studies might be related to the different study populations. In the study of Duan *et al.* [23], all enrolled patients were admitted to the respiratory ICU with acute respiratory failure of different etiologies and only a small subgroup of patients had heart failure, while in this present study, all of our enrolled patients had systolic cardiac dysfunction.

This study used the APACHE II score to evaluate the studied patients. Our results showed that the NIV failure group had a significantly higher mean APACHE II score than the NIV success group (17.5 $\pm$ 3.5 *vs.* 11.3 $\pm$ 3.7, $p < 0.001$). Although the APACHE II score could not be included in multivariate analysis because of collinearity with the HACOR score, it was found to be a predictor of NIV failure in a regression model. These findings were concordant with that of Rodríguez *et al.* [27], who reported that the APACHE II was significantly higher in the NIV failure group than in the NIV success group (17 (13–22) *vs.*14 (10–19), $p < 0.001$) and was a predictor of NIV failure (OR: 1.05, 95% CI: 1.03–1.08, $p < 0.001$). Our results also showed that the APACHE II score had a better distinguishing power for predictive NIV failure (AUROC 0.879) than HACOR (AUROC 0.791) at NIV initiation. Duan *et al.* [23] also investigated the APACHE II score in their NIV failure and NIV success groups (19 $\pm$ 6 *vs.* 16 $\pm$ 5, respectively ($p < 0.01$)) and upon comparing their HACOR score at T1 with different APACHE II scores, they found that HACOR had a good distinguishing power regardless of APACHE II for NIV failure.

We used the SOFA score to assess the disease severity of the enrolled patients. The SOFA score is a simple score that can be used for assessment and follow-up of different organ dys-

functions and was shown to have a satisfactory performance in different groups of critically ill patients [40–42]. Our NIV success group demonstrated a significantly lower mean SOFA score with a decreasing trend after 48 hours of NIV initiation than the NIV failure group. Regression analyses showed that SOFA was an independent predictor of NIV failure (OR: 4.52, 95% CI: 2.59–7.88, $p < 0.001$). Moreover, the initial SOFA score demonstrated good distinguishing power for predicting NIV failure (AUROC, 0.882) at a cutoff of 7, with a sensitivity of 90.6%, specificity of 81.5%, and accuracy of 84.2%. Our findings were similar to that of Rodríguez *et al.* [27], who also reported a higher SOFA score in the NIV failure group than in the NIV success group (7 (4–9) *vs.* 4 (3–6), respectively ($p < 0.001$)). Rodríguez *et al.* [27] also reported that patients with SOFA ≥ 5 had a 3-fold risk of NIV failure (OR = 3.3, 95% CI 2.4–4.5, $p < 0.001$) compared to those with SOFA <5 and that this cutoff value could be used as the first line of branching of chi-squared automatic interaction detection (CHAID) analysis for NIV failure.

In this present study, blood lactate was used as a marker of tissue hypoperfusion. Our results found significantly higher mean blood lactate levels in the NIV failure group at NIV initiation and 12 and 24 hours later compared to the NIV success groups. Blood lactate was also identified as an independent predictor of NIV failure (OR: 9.35, 95% CI: 5.32–43.26, $p < 0.001$) with good discriminating power for NIV failure at the 3 points of measurements, namely, NIV initiation (AUROC = 0.856), 12 hours later (AUROC = 0.815) and 24 hours later (AUROC = 0.954). Liengswangwong *et al.* [43] investigated NIV failure at their emergency department and found that it was the most significant predictor of NIV failure. Blood lactate is a marker of tissue hypoxia, organ hypoperfusion and respiratory muscle fatigue and has been linked to mortality in different clinical conditions [44–47].

We used quantitative LUS for accurate assessment of patients with systolic cardiac dysfunctions, diagnosis of pneumonia, pleural effusion, and pulmonary edema. Quantitative LUS was performed at NIV initiation and 12 and 24 hours later. We observed that patients with NIV failure had significantly higher mean LUS scores without a decrementing pattern with NIV and diuresis than the NIV success group. Quantitative LUS was found to be a predictor of NIV failure in our multivariate regression model with good distinguishing power at NIV initiation (AUROC = 0.728), T12 (AUROC = 0.727) and T24 (AUROC = 0.79). Recently, Biasucci *et al.* [48] conducted a prospective study and reported that the LUS score of patients with NIV failure was significantly higher than in those with successful NIV, and it was correlated with the need for invasive mechanical ventilation and ICU stay with good distinguishing power (AUROC = 0.95). Quantitative LUS was shown to be a valuable tool for rapid assessment and diagnosis of pneumonia, pulmonary edema, asthma, and chronic obstructive pulmonary disease exacerbation [49, 50].

NIV is widely used to support cardiac patients, and a rapid assessment of patients with cardiac dysfunction using the APACHE II, SOFA, HACOR and LUS scores and blood lactate levels could help predict their risk of NIV failure and avoid delayed invasive ventilation, which has been associated with increased mortality.

5. Conclusion

Our results showed that high initial HACOR and SOFA scores, persistent hyperlactatemia and a non-decrementing pattern of LUS score were associated with early NIV failure in patients with heart failure presenting with CAP. Thus, these clinical and paraclinical variables could be used for early decision-making regarding invasive ventilation. Also, we recommend larger prospective studies to validate our results.

6. Limitations

Although this was a prospective multicenter study, the management and diagnosis of NIV failure and decision of invasive mechanical ventilation were based on the attending physicians without a standardized protocol. In addition, blood lactate measurements were used, and we did not calculate the lactate clearance of the patients. Due to the overlapping manifestations of heart failure and sepsis, we could not report the cardiac events that occurred during the ICU stay. Lastly, we did not use a standardized protocol to follow up on inflammatory and cardiac biomarkers.

ABBREVIATIONS

APACHE II: Acute Physiology and Chronic Health Evaluation II; AKI: Acute Kidney Injury; CI: Confidence interval; CKD: Chronic Kidney Disease; CPAP: Continuous Positive Airway Pressure; HACOR: Heart rate Acidosis Consciousness Oxygenation and Respiratory rate; LUS: Lung Ultrasound; NIV: Non-Invasive Ventilation; OR: Odds ratio; SOFA: Sequential Organ Failure Assessment; INR: International Normalized Ratio; PPV: Positive Predictive Value; PEEP: Positive End Expiratory Pressure; NPV: Negative Predictive Value.

AVAILABILITY OF DATA AND MATERIALS

The data presented in this study are available on reasonable request from the corresponding author.

AUTHOR CONTRIBUTIONS

ML and WA participated in study design, registration, data collection and analysis and manuscript writing. MAM, ME and TM participated in study conduction, data collection and interpretation. All authors read and approved the publication.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

This multicenter prospective observational study was performed at the critical care units of 5 different hospitals, including a university hospital, and was approved by the Ethics Committee and Institutional Review Board, with registration number ISRCTN14641518. Informed consents have been taken from all enrolled patients.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

REFERENCES

[1] Corrales-Medina VF, Musher DM, Wells GA, Chirinos JA, Chen L, Fine MJ. Cardiac complications in patients with community-acquired pneumonia: incidence, timing, risk factors, and association with short-term mortality. Circulation. 2012; 125: 773–781.

[2] Corrales-Medina VF, Madjid M, Musher DM. Role of acute infection in triggering acute coronary syndromes. The Lancet. Infectious Diseases. 2010; 10: 83–92.

[3] Masip J, Peacock WF, Price S, Cullen L, Martin-Sanchez FJ, Seferovic P, *et al*. Indications, and practical approach to non-invasive ventilation in acute heart failure. European Heart Journal. 2018; 39: 17–25.

[4] Park JJ, Choi D, Yoon C, Oh I, Lee JH, Ahn S, *et al*. The prognostic value of arterial blood gas analysis in high-risk acute heart failure patients: an analysis of the Korean Heart Failure (KorHF) registry. European Journal of Heart Failure. 2015; 17: 601–611.

[5] Mebazaa A, Pang PS, Tavares M, Collins SP, Storrow AB, Laribi S, *et al*. The impact of early standard therapy on dyspnoea in patients with acute heart failure: the URGENT-dyspnoea study. European Heart Journal. 2010; 31: 832–841.

[6] Tobin MJ. Advances in mechanical ventilation. New England Journal of Medicine. 2001; 344: 1986–1996.

[7] Lin M, Yang Y, Chiang H, Chang M, Chiang BN, Cheitlin MD. Reappraisal of continuous positive airway pressure therapy in acute cardiogenic pulmonary edema. Chest. 1995; 107: 1379–1386.

[8] Bradley TD, Holloway RM, McLaughlin PR, Ross BL, Walters J, Liu PP. Cardiac output response to continuous positive airway pressure in congestive heart failure. American Review of Respiratory Disease. 1992; 145: 377–382.

[9] Jolliet P, Abajo B, Pasquina P, Chevrolet JC. Non-invasive pressure support ventilation in severe community-acquired pneumonia. Intensive Care Med. 2001; 27: 812–821.

[10] He H, Sun B, Liang L, Li Y, Wang H, Wei L, *et al*. A multicenter RCT of noninvasive ventilation in pneumonia-induced early mild acute respiratory distress syndrome. Critical Care. 2019; 23: 300.

[11] Antonelli M, Conti G, Esquinas A, Montini L, Maggiore SM, Bello G, *et al*. A multicenter survey on the use in clinical practice of non-invasive ventilation as a first line intervention for acute respiratory distress syndrome. Critical Care Medicine. 2007; 35: 18–25.

[12] Patel BK, Wolfe KS, Pohlman AS, Hall JB, Kress JP. Effect of noninvasive ventilation delivered by helmet *vs.* face mask on the rate of endotracheal intubation in patients with acute respiratory distress syndrome. JAMA. 2016; 315: 2435.

[13] Bellani G, Laffey JG, Pham T, Madotto F, Fan E, Brochard L, *et al*. Noninvasive ventilation of patients with acute respiratory distress syndrome. Insights from the LUNG SAFE study. American Journal of Respiratory and Critical Care Medicine. 2017; 195: 67–77.

[14] Booth A. Clear and present questions: formulating questions for evidence based practice. Library Hi Tech. 2006; 24: 355–368.

[15] Ferrer M, Esquinas A, Leon M, Gonzalez G, Alarcon A, Torres A. Noninvasive ventilation in severe hypoxemic respiratory failure. American Journal of Respiratory and Critical Care Medicine. 2003; 168: 1438–1444.

[16] Agarwal R, Handa A, Aggarwal AN, Gupta D, Behera D. Outcomes of non-invasive ventilation in acute hypoxemic respiratory failure in a respiratory intensive care unit in north India. Respiratory Care. 2009; 54: 1679–1687.

[17] Carron M, Freo U, Zorzi M, Ori C. Predictors of failure of noninvasive ventilation in patients with severe community-acquired pneumonia. Journal of Critical Care. 2010; 25: 540.e9–540.e14.

[18] Muriel A, Peñuelas O, Frutos-Vivar F, Arroliga AC, Abraira V, Thille AW, *et al*. Impact of sedation and analgesia during noninvasive positive pressure ventilation on outcome: a marginal structural model causal analysis. Intensive Care Medicine. 2015; 41: 1586–1600.

[19] Yoshida Y, Takeda S, Akada S, Hongo T, Tanaka K, Sakamoto A. Factors predicting successful noninvasive ventilation in acute lung injury. Journal of Anesthesia. 2008; 22: 201–206.

[20] Masclans JR, Pérez M, Almirall J, Lorente L, Marqués A, Socias L, *et al*. Early non-invasive ventilation treatment for severe influenza pneumonia. Clinical Microbiology and Infection. 2013; 19: 249–256.

[21] Ozyilmaz E, Ugurlu AO, Nava S. Timing of noninvasive ventilation failure: causes, risk factors, and potential remedies. BMC Pulmonary Medicine. 2014; 14: 19.

[22] Antonelli M, Conti G, Moro M, Esquinas A, Gonzalez-Diaz G, Confalonieri M, *et al*. Predictors of failure of noninvasive positive pressure ventilation in patients with acute hypoxemic respiratory failure: a multi-center study. Intensive Care Medicine. 2001; 27: 1718–1728.

[23] Duan J, Han X, Bai L, Zhou L, Huang S. Assessment of heart rate, acidosis, consciousness, oxygenation, and respiratory rate to predict noninvasive ventilation failure in hypoxemic patients. Intensive Care Medicine. 2017; 43: 192–199.

[24] Duan J, Wang S, Liu P, Han X, Tian Y, Gao F, *et al*. Early prediction of non-invasive ventilation failure in COPD patients: derivation, internal validation, and external validation of a simple risk score. Annals of Intensive Care. 2019; 9: 108.

[25] Todur P, Souvik Chaudhuri FNB Critical Care, Vedaghosh Amara FNB Critical Care, Srikant N, Prakash P. Correlation of oxygenation and radiographic assessment of lung edema (RALE) score to lung ultrasound score (LUS) in acute respiratory distress syndrome (ARDS) patients in the intensive care unit. Canadian Journal of Respiratory Therapy. 2021; 57: 53–59.

[26] Soliman SB, Ragab F, Soliman RA, Gaber A, Kamal A. Chest ultrasound in predication of weaning failure. Open Access Macedonian Journal of Medical Sciences. 2019; 7: 1143–1147.

[27] Rodríguez A, Ferri C, Martin-Loeches I, Díaz E, Masclans JR, Gordo F, *et al*. Risk factors for noninvasive ventilation failure in critically ill subjects with confirmed influenza infection. Respiratory Care. 2017; 62: 1307–1315.

[28] Ozyilmaz E, Ugurlu AO, Nava S. Timing of noninvasive ventilation failure: causes, risk factors, and potential remedies. BMC Pulmonary Medicine. 2014; 14: 19.

[29] Confalonieri M. A chart of failure risk for noninvasive ventilation in patients with COPD exacerbation. European Respiratory Journal. 2005; 25: 348–355.

[30] Moretti M. Incidence and causes of non-invasive mechanical ventilation failure after initial success. Thorax. 2000; 55: 819–825.

[31] Rana S, Jenad H, Gay PC, Buck CF, Hubmayr RD, Gajic O. Failure of non-invasive ventilation in patients with acute lung injury: observational cohort study. Critical Care. 2006; 10: R79.

[32] Nava S, Hill N. Non-invasive ventilation in acute respiratory failure. The Lancet. 2009; 374: 250–259.

[33] Ferrer M, Cosentini R, Nava S. The use of non-invasive ventilation during acute respiratory failure due to pneumonia. European Journal of Internal Medicine. 2012; 23: 420–428.

[34] Sarnoff SJ, Braunwald E, Welch GH, Case RB, Stainsby WN, Macruz R. Hemodynamic determinants of oxygen consumption of the heart with special reference to the tension-time index. American Journal of Physiology-Legacy Content. 1957; 192: 148–156.

[35] Ferro G, Duilio C, Spinelli L, Liucci GA, Mazza F, Indolfi C. Relation between diastolic perfusion time and coronary artery stenosis during stress-induced myocardial ischemia. Circulation. 1995; 92: 342–347.

[36] Suffredini AF, Fromm RE, Parker MM, Brenner M, Kovacs JA, Wesley RA, *et al*. The cardiovascular response of normal humans to the administration of endotoxin. New England Journal of Medicine. 1989; 321: 280–287.

[37] Maeder M, Fehr T, Rickli H, Ammann P. Sepsis-associated myocardial dysfunction. Chest. 2006; 129: 1349–1366.
[38] Habimana R, Choi I, Cho HJ, Kim D, Lee K, Jeong I. Sepsis-induced cardiac dysfunction: a review of pathophysiology. Acute and Critical Care. 2020; 35: 57–66.
[39] Kakihana Y, Ito T, Nakahara M, Yamaguchi K, Yasuda T. Sepsis-induced myocardial dysfunction: pathophysiology and management. Journal of Intensive Care. 2016; 4: 22.
[40] Ferreira FL. Serial evaluation of the SOFA score to predict outcome in critically ill patients. JAMA. 2001; 286: 1754.
[41] Laimoud M, Alanazi M. The validity of SOFA score to predict mortality in adult patients with cardiogenic shock on venoarterial extracorporeal membrane oxygenation. Critical Care Research and Practice. 2020; 2020: 1–9.
[42] Lambden S, Laterre PF, Levy MM, Francois B. SOFA score—development, utility and challenges of ac-curate assessment in clinical trials. Critical Care. 2019; 23: 374.
[43] Liengswangwong W, Yuksen C, Thepkong T, Nakasint P, Jenpanitpong C. Early detection of non-invasive ventilation failure among acute respiratory failure patients in the emergency department. BMC Emergency Medicine. 2020; 20: 80.
[44] Schiavo A, Renis M, Polverino M, Iannuzzi A, Polverino F. Acid–base balance, serum electrolytes and need for non-invasive ventilation in patients with hypercapnic acute exacerbation of chronic obstructive pulmonary disease admitted to an internal medicine ward. Multidisciplinary Respiratory Medicine. 2016; 11: 23.
[45] Laimoud M, Alanazi M. The clinical significance of blood lactate levels in evaluation of adult patients with veno-arterial extracorporeal membrane oxygenation. The Egyptian Heart Journal. 2020; 72: 74.
[46] Shapiro NI, Howell MD, Talmor D, Nathanson LA, Lisbon A, Wolfe RE, *et al*. Serum lactate as a predictor of mortality in emergency department patients with infection. Annals of Emergency Medicine. 2005; 45: 524–528.
[47] Schollin-Borg M, Nordin P, Zetterström H, Johansson J. Blood lactate is a useful indicator for the medical emergency team. Critical Care Research and Practice. 2016; 2016: 1–7.
[48] Biasucci DG, Buonsenso D, Piano A, Bonadia N, Vargas J, Settanni D, *et al*. Lung ultrasound predicts non-invasive ventilation outcome in COVID-19 acute respiratory failure: a pilot study. Minerva Anestesiologica. 2021; 87: 1006–1016.
[49] Staub LJ, Mazzali Biscaro RR, Kaszubowski E, Maurici R. Lung ultrasound for the emergency diagnosis of pneumonia, acute heart failure, and exacerbations of chronic obstructive pulmonary disease/asthma in adults: a systematic review and meta-analysis. The Journal of Emergency Medicine. 2019; 56: 53–69.
[50] Long L, Zhao HT, Zhang ZY, Wang GY, Zhao HL. Lung ultrasound for the diagnosis of pneumonia in adults: a meta-analysis. Medicine. 2017; 96: e5713.

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