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Evaluation of factors affecting the success of non invasive mechanical ventilation in acute cardiogenic pulmonary edema in the emergency department

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Abstract:

OBJECTIVES: The aim of this study was to evaluate the factors associated with non-invasive mechanical ventilation (NIMV) failure in acute cardiogenic pulmonary edema (ACPE) diagnosed in the emergency department.

METHODS: This study was prospectively conducted at the Ege University Faculty of Medicine ED between February 19, 2021 and December 01, 2021. Patients who received NIMV with ACPE were included. Patients' clinical and laboratory parameters, treatments, NIMV mode, and settings were recorded. The primary endpoint was NIMV failure (intubation within 24 h). Secondary endpoints were early NIMV failure, early mortality (within 24 h), and in-hospital mortality. Early NIMV failure was defined as follows: if the patient had a respiratory rate of more than 25 per minute, oxygen saturation below 90%, $PaCO_2$ >50 mmHg in blood gas, and pH <7.35, 1 h after starting NIMV.

RESULTS: Out of 347 patients in this study, 34 (10.7%) of them intubated within 24 h. Female sex percentage was 48.7%. Median age was 73 years. Risk factors for NIMV failure were respiratory rate >40.5, systolic blood pressure <122.5 mmHg, Glasgow Coma Score <14, pH <7.21, lactate level >5.2 mmol/L, base excess <−4.5 mmol/L, B-type natriuretic peptide level >3007 pg/mL (respectively area under the curve values; 0.723, 0.693, 0.739, 0.721, 0.690, 0.698, and 0.616).

CONCLUSION: Signs of hypoperfusion such as low systolic blood pressure (<122.5 mmHg) and high lactate (lactate level >5.2 mmol/L) are risk factors for NIMV failure. Evaluation of initial vital signs and arterial blood gas parameters is significantly important for prediction of NIMV success in ED.

Keywords:

Emergency department, heart failure, noninvasive ventilation, pulmonary edema

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Introduction

Acute cardiogenic pulmonary edema (ACPE) is a life-threatening condition that occurs with increased pulmonary congestion associated with systolic dysfunction in patients with acute heart failure and causes acute respiratory failure. Noninvasive mechanical ventilation (NIMV) may be required in patients who do not respond to initial treatment and/or have severe respiratory failure (respiratory rate >25/min, oxygen saturation <90%), or in more severe patients endotracheal intubation and mechanical ventilation may be required. NIMV decreases intubation and mortality rates

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Box-ED section

What is already known on the study topic?

- Noninvasive mechanical ventilation (NIMV) is frequently utilized in emergency departments for the management of ACPE. Despite its widespread use, the identification of specific risk factors for NIMV failure in this patient population remains insufficiently explored. Current literature predominantly focuses on the immediate benefits of NIMV, such as reducing intubation rates, yet there is a significant gap in understanding which patients are more likely to experience adverse outcomes.

What is the conflict on the issue? Is it important for readers?

- The primary conflict surrounding the use of NIMV in ACPE lies in the identification and management of risk factors for NIMV failure. This issue is pivotal as it influences clinical outcomes and resource allocation in emergency care settings. There remains a contentious debate among clinicians and researchers regarding the optimal timing, patient selection, and intervention strategies to minimize failure rates.

How is this study structured?

- This study was prospectively conducted at the Ege University Faculty of Medicine ED between February 19, 2021 and December 01, 2021. Patients who received NIMV with ACPE were included. Patients' clinical and laboratory parameters, treatments, NIMV mode, and settings were recorded. The primary endpoint was NIMV failure (intubation within 24 h). Secondary endpoints were early NIMV failure, early mortality (within 24 h), and in-hospital mortality. Early NIMV failure was defined as follows: if the patient had a respiratory rate of >25 per min, oxygen saturation <90%, $PaCO_2$>50 mmHg in blood gas, and pH <7.35, 1 h after starting NIMV.

What does this study tell us?

- Predicting potential failure before the application of NIMV is crucial. Absence of hypertension and the presence of prominent signs of hypoperfusion are key risk factors for NIMV failure. Initial vital signs and arterial blood gas parameters play a critical role in predicting NIMV success.

of patients by increasing oxygenation and decreasing respiratory workload.[1-3]

It is recommended that NIMV (continuous positive airway pressure [CPAP] or bilevel positive airway pressure [BPAP]) to be applied as soon as possible in patients with ACPE whose respiratory rate is >25 per minute and oxygen saturation is <90%. If respiratory failure causes hypoxemia (PaO_2 < 60 mmHg), hypercarbia ($PaCO_2$ >50 mmHg) and acidosis (pH <7.35) and cannot be treated with NIMV, it is recommended that the patient to be intubated and followed up with invasive mechanical ventilation (IMV).[1]

It is known that the use of NIMV in respiratory failure due to ACPE reduces the respiratory distress of the patient and reduces intubation and mortality rates.[4] In a meta-analysis conducted by Berbenetz *et al*., it was found that the use of NIMV for ACPE provides a mortality benefit compared to standard medical treatment. However, there is not enough data on the factors affecting the success of NIMV in the ED.[2]

The majority of studies on the success of NIMV have been conducted in patient populations in intensive care units (ICU) and by including causes of respiratory failure such as chronic obstructive pulmonary disease (COPD) exacerbation and pneumonia.[5-8] As the patient population in ED differs from ICUs, ACPE also differs from other respiratory failure causes in terms of disease course and treatment. Studies on the success of NIMV in patients with ACPE in the ED are limited. Objective criteria suitable for use in the ED continue to be needed to predict NIMV failure in this patient group. In our study, we aimed to evaluate the factors associated with NIMV failure in patients followed up with the diagnosis of ACPE in the ED.

Methods

Study design

The study was conducted as a prospective observational study. Ethics committee approval for the study was obtained from the Ege University Clinical Research Ethics Committee (21-2.1T/44, February 19, 2021). Patient recruitment was started following ethics committee approval. Informed consent was obtained from all patients included in the study or their legal representatives. All procedures were carried out in accordance with the relevant ethical rules.

Study population

Patients aged 18 years or older who presented to the emergency department with sudden onset dyspnea between February 19, 2021, and December 1, 2021, and who provided consent, were included in the study if they had findings of congestion on chest X-ray or pulmonary edema on thoracic computed tomography and were diagnosed with acute cardiogenic pulmonary edema (ACPE) based on examination findings, B-Type natriuretic peptide (BNP) results, and the primary provider's assessment, with a decision made to apply noninvasive mechanical ventilation (NIMV). Only patients who met least one of the following criteria indicative of acute decompensated heart failure were included in the study: use of accessory or abdominal

muscles, respiratory rate >25/minute (min), oxygen saturation <90%, and arterial blood gas pH value <7.35. Exclusion criteria included patients who:

- Were not started on NIMV within the 1st hour of hospital presentation
- Experienced cardiac or respiratory arrest before or upon arrival at the hospital
- Had facial trauma, deformity, or upper airway obstruction
- Had upper gastrointestinal bleeding or pneumothorax
- Had a Glasgow Coma Scale (GCS) score < 12
- Suffered from life-threatening multiorgan failure or cardiac arrhythmia
- Used home mechanical ventilators
- Had chronic kidney failure and were noncompliant with the routine dialysis program [Figure 1].

Data

The demographic data of the patients included in the study (age, sex, date of admission), comorbidities, vital signs at the time of presentation, GCS score, arterial blood gas, biochemistry and hemogram parameters and the mode of NIMV used (CPAP, BPAP) were recorded in the study data form. The vital signs and arterial blood gas parameters were measured again 1 h after the initiation of NIMV. The treatments administered during the ED follow-up were also recorded.

Noninvasive mechanical ventilation protocol

NIMV was applied using the Philips Respironics Trilogy 202 ventilator (Amsterdam, Netherlands) with a PerforMax oronasal mask in our ED. In our ED, the routine practice is to use the S/T (spontaneous/timed) mode of the ventilator for BPAP, and the CPAP mode is preferred for patients receiving CPAP. This ventilator has an AVAPS option, but this mode was not used in the study. During the study process, there was no intervention in the requested tests and administered treatments. The selection of NIMV modes was made by the patient's primary provider.

A standardized procedure for NIMV application is followed in our clinic. The initial CPAP pressure for patients is set within the range of 5–10 cmH_2O and can be increased up to a maximum of 15 cmH_2O. For patients receiving BPAP, the inspiratory positive airway pressure is set at 8 cmH_2O and the expiratory positive airway pressure is set at 4 cmH_2O initially. The inspiratory pressure can be increased up to a maximum of 20 cmH_2O, and the expiratory pressure can be increased up to a maximum of 10 cmH_2O.

Definitions and outcomes

The diagnosis of ACPE was established based on the patient's clinical symptoms, lung imaging findings and BNP levels. However, the primary provider's clinical judgment was the main factor in diagnosing ACPE. One hour after starting NIMV, if the patient had a respiratory rate of over 25 breaths per minute, oxygen saturation below 90%, $PaCO_2$>50 mmHg, or pH <7.35 in the blood gas analysis, it was defined as early NIMV failure.[2] The primary endpoint of the study was determined as the need for intubation within 24 h, and patients who required intubation were considered NIMV failure. The secondary endpoints of the study were early NIMV failure, early mortality (within the first 24 h of ED presentation), and in-hospital mortality.

Sample size

Adult ED of our hospital receives approximately 200,000 patients per year. A previous study conducted in our ED revealed that 190 patients received NIMV due to ACPE within 1 year.[9] The study duration was set to 1 year. Taking into account potential dropouts, it was planned to include a minimum of 200 patients in the study.

Statistical analysis

The data were recorded in the "Statistical Package for Social Sciences for MAC 27.0" (IBM Corporation, Armonk, New York, United States) program. The normal distribution was tested using the Kolmogorov–Smirnov test. Normally distributed data were presented as mean and standard deviation, while nonnormally distributed data were presented as median and interquartile range (IQR). Comparisons of numerical variables between independent groups were performed using the Student's *t*-test and Mann–Whitney *U* test. The categorical variables between independent groups were tested using the Chi-square or Fisher's exact tests. Receiver operating characteristic (ROC) analysis was performed to evaluate the predictive values for NIMV failure. The Youden Index was used to determine the optimal cutoff points.

Results

The study was conducted with 347 patients. Of these, 178 (51.3%) were male. The median age was 73 (IQR 25–75; 63–86). The most common comorbidity observed was hypertension, which was present in 75.8% of the patients.

NIMV failure was observed in 37 (10.7%) patients, early NIMV failure in 191 (55.1%) patients, early mortality in 15 (4.3%) patients, and in-hospital mortality in 62 (17.9%) patients. It was found that 37 patients (10.7%) required intubation within 24 h.

In the group of patients with NIMV failure, active malignancy was more frequently observed ($P = 0.007$).

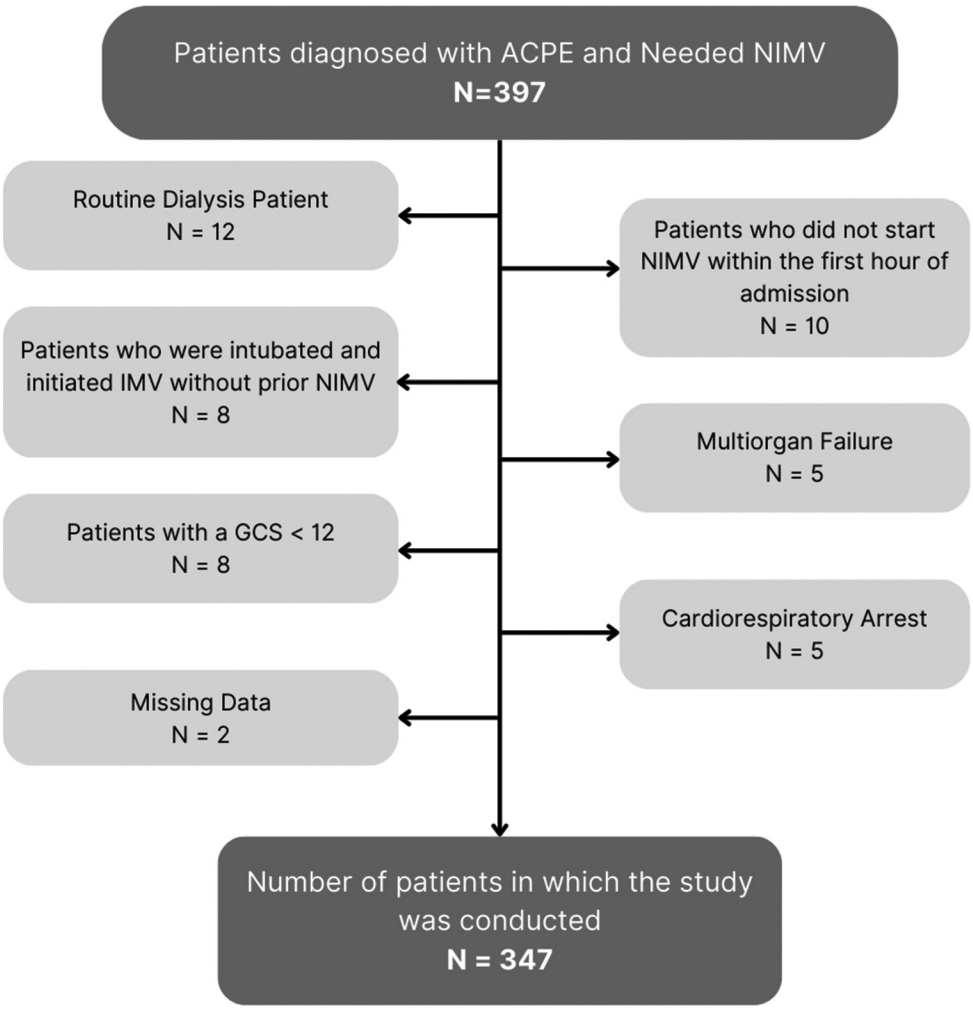

Figure 1: Flow Chart of the study (ACPE: Acute cardiogenic pulmonary edema, NIMV: Non invasive mechanical ventilation, IMV: Invasive mechanical ventilation, GCS: Glasgow Coma Score)

In the group of patients with successful NIMV, hypertension and COPD were more common ($P = 0.005$ and $P = 0.024$, respectively). Systolic blood pressure (SBP) at NIMV initiation (0 h) and at 1 h (1. h) was significantly higher in the successful NIMV group ($P < 0.001$ and $P = 0.015$, respectively). Respiratory rate, both at 0 h and 1 h, was higher in the NIMV failure group ($P < 0.001$). Among the laboratory parameters, PCO2 at 1. h, pH at 0 h and 1 h, lactate at 0 h and 1 h, troponin, and BNP levels were higher in the NIMV failure group. pH and BE at 0 h and 1 h, and HCO_3 at 1 h were significantly lower in the NIMV failure group [Table 1].

In the comparison between early NIMV groups, active malignancy was more common in the failure group, while atrial fibrillation was more common in the successful group ($P = 0.045$ and $P = 0.008$, respectively). Respiratory rate (RR) was higher in the failure group at both 0 h and 1 h ($P < 0.001$). Other clinical and laboratory parameters are presented in Table 1.

Regarding the administered treatments, vasodilators ($P = 0.003$) and diuretics ($P = 0.018$) were less frequently used in the NIMV failure group, while inotropes were more frequently used ($P < 0.001$). BPAP mode was more commonly preferred in the NIMV failure group ($P < 0.001$). In the early NIMV failure group, inotropes ($P = 0.005$) and BPAP mode ($P < 0.001$) were more frequently used. In addition, ultrafiltration was significantly more common in this group ($P = 0.009$). The administered treatments and mortality data according to NIMV groups are presented in Table 2.

Parameters that showed significant differences between NIMV groups were evaluated using ROC analysis. The AUC values for RR at 1 h were 0.835 (95% confidence interval (CI): 0.756–0.915), for pH at 1 h were 0.827 (95% CI: 0.746–0.907), and for lactate at 1. h were 0.759 (95% CI: 0.660–0.858). According to the Youden index, the optimal cutoff values were determined as 28.5/min for RR at 1 h, 7.26 for pH at 1 h, and 2.4 mmol/L for lactate at 1 h [Table 3].

Table 1: Demographic and clinical parameters in noninvasive mechanical ventilation failure groups

	NIMV failure			NIMV early failure		
	Success (*n*=310), *n* (%)	Failure (*n*=37), *n* (%)	*P*	Success (*n*=156), *n* (%)	Failure (*n*=191), *n* (%)	*P*
Age (years), median (IQR)	73 (63–82)	72 (65–84)	0.986	72 (65–80)	76 (65–82)	0.428
Gender, female	148 (47.7)	21 (56.8)	0.300	87 (55.8)	82 (42.9)	0.800
Comorbidities						
DM	149 (48.1)	16 (43.2)	0.579	79 (50.6)	85 (44.5)	0.274
HT	241 (77.4)	21 (56.8)	0.005	122 (78.2)	139 (72.8)	0.278
CAD	214 (69)	23 (62.2)	0.396	110 (70.5)	126 (66)	0.404
CHF	217 (70)	22 (59.5)	0.191	113 (72.4)	125 (65.4)	0.184
COPD	76 (34.5)	3 (8.1)	0.024	36 (97.3)	43 (22.5)	0.922
AF	107 (34.5)	8 (21.6)	0.115	63 (40.4)	51 (26.7)	0.008
CKD	46 (14.8)	6 (16.2)	0.824	21 (13.5)	30 (15.7)	0.543
Malignancy	12 (3.9)	6 (16.2)	0.007	4 (2.7)	14 (7.3)	0.045
Vital signs, median (IQR)						
RR - 0 h	34 (30–39)	41 (35–44)	<0.001	32 (30–36)	35 (30–40)	<0.001
RR - 1 h	24 (20–28)	29 (28–33)	<0.001	21 (19–24)	28 (24–31.75)	<0.001
SBP - 0 h	169 (149–194)	122 (110–158)	<0.001	161 (138–185)	168 (149–195)	0.505
SBP - 1 h	136 (124–152)	114 (110–136)	0.015	133 (123–151)	137 (117–150)	0.520
DBP - 0 h	97 (83–112)	85 (73–98)	0.062	90 (80–108)	96 (83–114)	0.916
DBP - 1 h	79 (69–92)	83 (62–95)	0.173	76 (68–90)	81 (71–93)	0.392
PR - 0 h	105 (85–121)	117 (88–136)	0.795	97 (83–121)	107 (91–122)	0.642
PR - 1 h	92 (77–106)	131 (96–152)	0.053	85 (69–107)	96 (83–113)	0.224
PI - 0 h	1.8 (0.9–3.6)	0.8 (0.1–1.6)	0.008	1.8 (0.9–4)	1.6 (0.8–2.8)	0.189
PI - 1 h	2.4 (1.1–4.3)	0.8 (0.2–1.8)	0.012	2.4 (1–4.5)	2.1 (1.1–3.4)	0.225
GCS - 0 h	15 (15–15)	15 (14–15)	<0.001	15 (15–15)	15 (15–15)	<0.001
GCS - 1 h	15 (15–15)	15 (13–15)	<0.001	15 (15–15)	15 (15–15)	<0.001
Laboratory findings, median (IQR)						
pH - 0 h	7.29 (7.23–7.35)	7.26 (7.23–7.41)	<0.001	7.31 (7.28–7.38)	7.26 (7.2–7.34)	<0.001
pH - 1 h	7.37 (7.3–7.41)	7.31 (7.08–7.38)	<0.001	7.4 (7.37–7.44)	7.32 (7.26–7.38)	<0.001
HCO_3 (mmol/L) - 0 h	23 (20–26.4)	15.3 (11.4–20.4)	0.002	22.3 (20–25.8)	23 (18.6–26.6)	0.001
HCO_3 (mmol/L) - 1 h	23.8 (20.2–27.2)	14.6 (12.9–22.4)	<0.001	22.85 (20–25.9)	24.1 (20–27.8)	<0.001
PCO_2 (mmHg) - 0 h	47 (40.5–59.6)	32.1 (25.8–42.8)	0.537	44 (37.7–50.8)	51 (38.6–65)	<0.001
PCO_2 (mmHg) - 1 h	42.7 (35.7–51.9)	43 (26.1–55.1)	0.019	36.4 (31.6–43.4)	48.2 (39.6–60.2)	0.506
Lactate (mmol/L) - 0 h	2.65 (1.6–3.825)	5.7 (3.5–9.6)	<0.001	2.6 (1.6–4)	2.9 (1.7–4.6)	<0.001
Lactate (mmol/L) - 1 h	1.6 (1.1–2.4)	4.4 (2.6–9.8)	<0.001	1.5 (1.1–2.2)	1.9 (1.2–2.9)	<0.001
BE (mmol/L) - 0 h	−1.4 (−4.625–1.3)	−8.8 (−15.1–−5.5)	<0.001	−2.1 (−4.9–0.6)	−1.5 (−7.8–1.8)	<0.001
BE (mmol/L) 0-1 h	−0.45 (−3.7–2.1)	−10.5 (−14.3–−3)	<0.001	−0.7 (−3.9–1.1)	−0.8 (−5.5–2.1)	<0.001
Troponin (pg/mL)	26 (16.3–41.5)	89.5 (26–560.5)	0.003	26 (19–38)	27.5 (15.3–58.5)	0.003
BNP (pg/mL)	3803 (1730–9908)	15,553 (3817–32,844)	0.035	3903 (1792–7818)	3976 (1732–13,019)	0.006
Creatinine (mg/dL)	1 (0.9–1.4)	1.35 (0.9–2.2)	0.310	1 (0.9–1.5)	1.1 (0.9–1.4)	<0.001
Hemoglobin (g/dL)	12.2 (10.4–14.3)	10.7 (8.3–12.5)	0.933	11.6 (10.3–14.2)	12.3 (10.4–14.1)	0.627

DM: Diabetes mellitus, HT: Hypertension, CAD: Coronary artery disease, CHF: Congestive heart failure, COPD: Chronic obstructive pulmonary disease, AF: Atrial fibrillation, CKD: Chronic kidney disease, RR: Respiratory rate, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, PR: Pulse rate, PI: Perfusion index, GCS: Glasgow Coma Scale, NIMV: Noninvasive mechanical ventilation, IQR: Interquartile range, BE: Base excess, BNP: B-type natriuretic peptide

Discussion

NIMV is the preferred respiratory support modality for ACPE patients in the ED if there are no contraindications. Although some studies have shown that ACPE patients have the lowest intubation rates among various patient groups requiring ventilation, it is important to note that not all patients respond to NIMV in a similar manner, and some may require intubation.[10] Failure to recognize patients requiring intubation early on can lead to adverse outcomes. Therefore, it is crucial to identify factors associated with NIMV failure and develop objective criteria to predict NIMV ventilation failure.

In studies conducted with ACPE patients in the ED, Aliberti *et al*. found an intubation rate of 2.6%, a mortality rate of 3% within the first 24 h, and an in-hospital mortality rate of 9%.[11] In studies conducted with ACPE patients in the ICU, Antonelli *et al*.[10] found an intubation rate of 10% and a mortality rate of 18% during hospitalization, while Luo *et al*.[12] reported an intubation rate of 37.3% and a mortality rate of

Table 2: Comparison of treatments and outcomes between noninvasive mechanical ventilation groups

	NIMV failure			NIMV early failure		
	Success (*n*=310), *n* (%)	Failure (*n*=37), *n* (%)	*P*	Success (*n*=156), *n* (%)	Failure (*n*=191), *n* (%)	*P*
Vasodilator	189 (61.0)	13 (35.1)	0.003	89 (57.1)	112 (58.6)	0.692
Diuretics	307 (99.0)	34 (91.9)	0.018	155 (99.4)	185 (96.4)	0.229
Inotrop	10 (3.2)	14 (37.8)	<0.001	4 (2.6)	20 (10.5)	0.005
NIMV mode						
CPAP	202 (65.2)	13 (35.1)	<0.001	118 (75.6)	96 (50.3)	<0.001
BPAP	108 (34.8)	24 (64.9)		38 (24.4)	94 (49.2)	
Ultrafiltration	9 (2.9)	3 (1)	0.125	1 (0.6)	11 (5.8)	0.009
Early mortality	1 (0.3)	14 (38.9)	<0.001[#]	0	15 (7.9)	<0.001
In hospital mortality	33 (10.7)	28 (75.7)	<0.001	9 (5.8)	52 (27.4)	<0.001
Early NIMV failure	155 (50)	36 (97.3)	<0.001	-	-	-
NIMV failure	-	-	-	1 (0.6)	36 (18.8)	<0.001

[#]Fisher's exact test. NIMV: Noninvasive mechanical ventilation, CPAP: Continuous positive airway pressure, BPAP: Bilevel positive airway pressure

Table 3: Receiver operating characteristic analysis data for noninvasive mechanical ventilation success

Parameter	AUC	95% CI	Cut point	Sensitivity	Specifity	*P*
RR - 0 h	0.723	0.632–0.813	40.5	53.3	84.6	<0.001
GCS - 0 h	0.739	0.635–0.843	14.0	54.1	91.0	<0.001
SBP - 0 h	0.693	0.589–0.797	122.5	43.2	90.6	<0.001
PI - 0 h	0.715	0.591–0.840	2.35	100	33.3	0.008
pH - 0 h	0.721	0.621–0.822	7.21	54.1	78.7	<0.001
HCO_3-0 h	0.655	0.543–0.767	20.4	62.2	66.8	0.003
Lactate - 0 h	0.690	0.590–0.791	5.2	51.4	85.2	<0.001
BE - 0 h	0.698	0.591–0.805	–4.5	68.6	65.3	<0.001
RR - 1 h	0.835	0.756–0.915	28.5	72.2	80.6	<0.001
SBP - 1 h	0.624	0.517–0.732	120.5	47.2	77.4	0.015
pH - 1 h	0.827	0.746–0.907	7.26	63.9	89.0	<0.001
HCO_3-1 h	0.685	0.571–0.799	17.1	44.4	91.6	<0.001
pCO_2-1 h	0.619	0.502–0.736	55.6	41.7	86.8	0.019
Lactate - 1 h	0.759	0.660–0.858	2.4	72.2	74.5	<0.001
BE - 1 h	0.724	0.621–0.827	–4.9	62.9	79.9	<0.001
BNP	0.616	0.500–0.732	3007	80	34.8	0.035

AUC: Area under the curve, RR: Respiratory rate, GCS: Glasgow Coma Scale, SBP: Systolic blood pressure, PI: Perfusion index, BE: Base excess, BNP: B-type natriuretic peptide, CI: Confidence interval

21.2% during the ICU stay. Similarly, our findings were in line with the rates reported in the literature, which strengthens the validity and applicability of our results.

In cases of acute heart failure developing on a hypertensive background, rapid clinical improvement is usually achieved after blood pressure control, which may explain the higher success rate of NIMV in patients with a known diagnosis of hypertension. Based on this, it should be considered that the success rate of NIMV may be lower in acute pulmonary edema cases not associated with a hypertensive background, and the prognosis of these patients may be worse. Antonelli *et al*. found a lower success rate of NIMV in patients with COPD compared to those without COPD in their study on hypoxic respiratory failure.[10] Luo *et al*. reported a higher failure rate of NIMV in patients with coronary artery disease and atrial fibrillation.[12] Since there is limited evidence on the impact of comorbidities on NIMV success in the literature, the findings in our study are important in this regard.

The presence of active malignancy was found to be higher in the NIMV failure group. Due to the scarcity of data in the literature, we think that our findings are significant.

In the study conducted by Luo *et al*., it was observed that the NIMV failure group had higher respiratory rates and lower systolic blood pressure.[12] In the same study, when vital signs measured 1 h after the initiation of NIMV were reviewed, the NIMV failure group had higher respiratory rates and lower heart rate and systolic blood pressure.[12] Liengswangwong *et al*. evaluated all patients who received NIMV for respiratory failure, regardless of etiology, in their ED study and reported that a heart rate above 110 beats per minute, systolic blood pressure below 110 mmHg, and oxygen saturation below 90% were associated with NIMV failure.[13] Lee

et al. in their study on patients undergoing NIMV in the emergency medical helicopter, found that a GCS <15 was associated with NIMV failure.[14] Similarly, in our study, when vital signs recorded 1 h after the initiation of NIMV were reviewed, the NIMV failure group had statistically significant higher respiratory rates and pulse rates, lower systolic blood pressure, and lower GCS. Considering these findings, we believe that vital signs can be used to predict NIMV success and evaluate the response to NIMV therapy.

In our study, the NIMV failure group had lower pH and HCO_3 values and higher lactate levels. These parameters reflect systemic hypoperfusion and are expected to indicate poor prognosis in ACPE patients. Similarly, Liengswangwong *et al*.[13] reported that a pH value <7.30 in arterial blood gas, Aliberti *et al*.[11] reported that a pH value <7.35 in arterial blood gas, Corrêa *et al*.[15] reported low bicarbonate and partial CO_2 levels, Luo *et al*.[12] reported high lactate levels, Liengswangwong *et al*.[13] reported a serum lactate level >4 mmol/L, and Corrêa *et al*.[15] reported a high serum lactate level were associated with NIMV failure.

In a study conducted by Nakano *et al*. with 714 patients diagnosed with acute heart failure, it was found that a base excess above 2.1 mEq/L increased 1-year mortality.[16] Guo *et al*. conducted a study with 5956 patients hospitalized for heart failure and reported that patients with a base excess between −3 and 2 mEq/L had lower 1-year mortality rates compared to patients with increased base excess (>2) or decreased base excess (<−3).[17] However, the relationship between base excess and NIMV success has not been adequately explored in the literature. Therefore, we believe that our findings are valuable in this regard.

In our study, we observed that patients in the NIMV failure group had statistically significantly increased BNP levels. Similarly, in a critical care study conducted by Luo *et al*. evaluating patients undergoing NIMV for ACPE, it was found that BNP levels >3350 pg/ml were associated with NIMV failure, which is consistent with our findings.[12] Taking these data into consideration, we believe that elevated BNP levels can be used as one of the criteria for the decision of invasive mechanical ventilation. Studies have shown that plasma BNP levels are strong markers for evaluating left ventricular ejection fraction and dimensions.[18] Elevated BNP levels may also have predictive value when determining the need for intubation as an indicator of more severe heart failure.

In our study, patients receiving vasodilator and diuretic therapy had higher NIMV success rates compared to those who did not receive these treatments, while patients receiving inotropes had a statistically significantly lower NIMV success rate. In patients with cardiogenic shock, respiratory failure is almost universally present, but due to patients' altered consciousness and inability to maintain their airway, providers often tend to prefer invasive mechanical ventilation.[3] The Euro Heart Failure Survey II reported an in-hospital mortality rate of 6.7% for patients admitted to the hospital for heart failure, while the mortality rate for those in cardiogenic shock was reported as 39.6%.[19] Antonelli *et al*. identified severe sepsis and septic shock as risk factors for NIMV failure.[10] Luo *et al*. reported that dopamine and noradrenaline were more frequently used in the treatment of patients in the NIMV failure group.[12] The low NIMV success rate in patients with cardiogenic shock in our study suggests an association with the poorer prognosis of the clinical condition, as reported in the literature compared to other heart failure clinics.

In our study, patients who were ordered CPAP mode as the NIMV mode by the primary provider had a statistically significantly higher NIMV success rate compared to those ordered BPAP mode. In the literature, randomized controlled trials and meta-analyses comparing CPAP and BPAP modes in patients with acute pulmonary edema did not find a significant difference in terms of intubation and mortality rates.[3,20,21] Similar to our study, in the study by Aliberti *et al*., it was found that the intubation rate was 2% in patients receiving CPAP, 6% in those receiving BPAP, and 1% in those receiving oxygen alone.[11] We believe that the findings of our study can be explained by the tendency of providers to prefer BPAP mode in patients with worse clinical parameters.

Limitations

The main limitation of our study is that the diagnosis of ACPE, the initiation of NIMV, selection of NIMV mode, and intubation decisions were made by the primary provider. There may have been differences in the therapies administered with NIMV in the management of acute decompensated heart failure and may have affected patient outcomes. In addition, our study was conducted at a single center. The lack of standard NIV settings in this study is a limitation, as NIV settings may vary between clinical practices and could influence treatment outcomes. Another limitation is the lack of inclusion of etiology of heart failure, severity of heart failure symptoms prior to ED presentation, and echocardiographic findings before and during admission. In addition, all active malignancies were grouped together due to their limited numbers.

Conclusion

In patients with nonhypertensive ACPE, the presence of malignancy, high respiratory rate, lactate, BE, BNP levels and low blood pressure, perfusion index, GCS,

pH, HCO_3, can be used as predictors of NIMV failure. Vital signs and blood gas parameters recorded 1 h after starting NIMV can be used to evaluate treatment success and make decisions regarding transitioning to invasive mechanical ventilation.

Author contribution statement
OAU: Data curation, Investigation, Methodology, Writing- Original draft preparation YAA: Data curation, Methodology, Conceptualization, Formal Analysis IU: Conceptualization, Formal analysis, Investigation, Methodology, Writing- review and editing FKA: Conseptualization, Methodology.

Conflicts of interest
None Declared.

Ethical approval
Our study received ethical approval from the Ege University Clinical Research Ethics Committee with decision number 21-2.1T/44 on February 19, 2021. Patient enrollment began after obtaining ethical approval. The study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki as reflected in *a priori* approval by the institution's human research committee.

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