

ORIGINAL RESEARCH

Clinical Prediction Score for Successful Weaning from Noninvasive Positive Pressure Ventilation (NIPPV) in Emergency Department; a Retrospective Cohort Study

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Abstract: **Introduction:** Due to the lack of in-hospital beds, some patients with acute cardiogenic pulmonary edema are initiated and weaned off noninvasive positive pressure ventilation (NIPPV) at the emergency department (ED). This study aimed to develop a clinical score to predict successful weaning from NIPPV in these patients. **Methods:** This retrospective cohort study was conducted on patients with acute cardiogenic pulmonary edema who received NIPPV at the ED of Ramathibodi Hospital, Bangkok, Thailand. Multivariable logistic regression analysis was used to develop a predictive model for weaning from NIPPV. **Results:** 355 patients with acute cardiogenic pulmonary edema treated with NIPPV were studied (107 (30.14%) failed to be weaned). The significant risk factors of weaning failure based on multivariate analysis were age > 75 years (OR: 3.1, 95% CI: 1.15–8.33, $p = 0.025$), pneumonia (OR: 2.72, 95% CI: 1.39–5.31, $p = 0.003$), pulse rate > 80 bpm before NIPPV (OR: 1.74, 95% CI: 1.04–2.91, $p = 0.033$), and a urinary output < 150 cc/h while using NIPPV (OR: 2.93, 95% CI: 1.74–4.91, $p < 0.001$). In addition, clinically significant risk factors for weaning from NIPPV were age 60–75 years, respiratory rate > 26 breaths/min before weaning and oxygen saturation of < 97% as assessed by pulse oximetry before weaning from NIPPV. Since the lowest coefficient obtained was 0.46, the scores were split into groups of 0.5 points for each factor. Based on the area under the receiver operating characteristic (ROC) curve (71.3% (95% CI: 66.0–75.7%)), the cut point of risk score was divided into the low-risk with positive likelihood ratio of 0.48 (95% CI 0.33–0.69, $P < 0.001$), the moderate-risk with positive likelihood ratio of 0.74 (95% CI 0.52–1.05, $P = 0.080$), and the high-risk group with positive likelihood ratio of 3.41 (95% CI 2.39–4.88, $P < 0.001$) for predicting weaning failure. **Conclusion:** In patients with acute cardiogenic pulmonary edema under the NIPPV, weaning is associated with a significant increasing risk of failure in age >75, presence of pneumonia, heart rate > 80 bpm before weaning, and urinary output < 150 cc/h during ventilation. Based on the designed model in this study, patients with score ≤ 3.5, 4–5, and > 5 points were in low, moderate, and severe risk of weaning failure, respectively.

Keywords: Noninvasive Ventilation; ventilator weaning; continuous positive airway pressure; emergency service, hospital; intubation

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1. Introduction

Acute cardiogenic pulmonary edema is a common cause of referring to emergency departments (EDs) worldwide. In the United States, approximately 6 million patients have acute cardiogenic pulmonary edema annually (1, 2). At Ramathibodi Hospital, Thailand, more than 450 patients are diagnosed with acute cardiogenic pulmonary edema annually and require a noninvasive ventilator.



The clinical diagnostic criteria for diagnosing acute cardiogenic pulmonary edema based on the European Society of Cardiology (ESC) guidelines are as follows: acute respiratory distress (acute increase in the work of breathing, considerable tachypnea, respiratory rate > 25 breaths/min, use of accessory muscles, or abdominal paradox), findings from a physical examination (crackles plus wheezing in the lungs or a third heart sound), and history of orthopnea and respiratory failure (oxygen saturation in room air by pulse oximetry < 60 mmHg, PaCO₂ > 45 mmHg, or PaO₂/fraction of inspired oxygen (FiO₂) < 300 mmHg) (3).

The diagnostic confirmation of acute cardiogenic pulmonary edema consists of at least two of the following: clear signs of pulmonary congestion on chest radiography or a computed tomography scan; multiple B-lines \geq 3; B-lines in two chest zones on each hemithorax as shown by lung ultrasound; elevated pulmonary capillary pressure on catheterization; increased total lung water on pulse contour and a thermodilution analysis system; signs of elevated filling pressure on echocardiography; and a significant elevation in natriuretic peptide concentrations (BNP > 400pg/ml or N-proBNP > 900pg/ml [or 1800pg/ml in > 75 years]).

There are various etiologies of acute cardiogenic pulmonary edema, such as cardiac ischemia, acute coronary disease, valvular heart disease, hypertensive emergency, arrhythmias, and tamponade (4). Symptoms of this condition include dyspnea, shortness of breath, leg edema, and desaturation (5-7). If a patient has mild symptoms of pulmonary edema, treatment involves oxygenation, a vasodilator drug, or a diuretic drug (1). In more severe cases, a noninvasive ventilator is applied to the patient to support ventilation and decrease the work of the breathing muscles.

Noninvasive ventilators continuously create positive airway pressure, decrease venous return to the heart, decrease afterload, reduce left ventricular pressure, and improve clinical outcomes in patients with acute cardiogenic pulmonary edema (8-10). Moreover, using noninvasive ventilators reduces intubation rate, the risk of post-intubation complications (e.g., infection, barotrauma, laryngeal edema, and tracheal stenosis), and hospital mortality in severe acute cardiogenic pulmonary edema (9, 11). Therefore, noninvasive ventilators are useful for treating acute cardiogenic pulmonary edema and have been suggested as the first-line strategy. When the patients' clinical outcome improves, they can be weaned off the noninvasive ventilator. Currently, Ramathibodi Hospital is experiencing the problem of a limitation of inpatient beds. This situation has led to ED overcrowding with critical patients receiving noninvasive ventilation, including those with acute cardiogenic pulmonary edema. Treatment is performed in a resuscitation zone, including weaning from noninvasive ventilation in acute cardiogenic edema. Noninvasive ventilation's rate of weaning failure (pa-

tients continue noninvasive ventilation or are intubated after weaning from noninvasive ventilation) is > 250 cases/year. Disadvantages of prolonged use of a noninvasive ventilator include gastric distension, aspiration, hypotension and coughing (12). A weaning failure can make patients feel uncomfortable. There is still a lack of evidence for using parameters to improve judgment and a successful outcome of weaning from noninvasive ventilation. This study aimed to develop a clinical score to predict the risk of failure to wean from noninvasive positive pressure ventilation (NIPPV) in patients with cardiogenic pulmonary edema.

2. Methods

2.1. Study design and setting

This is a retrospective cohort study to design a diagnostic prediction model, which was conducted on patients with acute cardiogenic pulmonary edema who received NIPPV for treatment at the ED of Ramathibodi Hospital, a university-affiliated super tertiary care hospital in Bangkok, Thailand, from January 2017 to December 2019. This study was approved by the Faculty of Medicine, Committee on Human Rights Related to Research Involving Human Subjects, Ramathibodi Hospital, Mahidol University (COA. NO MURA2020/972). The ethics committee waived obtaining consent for this research as the patients' medical records were used for data gathering and a statement covering patient data confidentiality and compliance with the Declaration of Helsinki was provided.

2.2. Participants

We included patients with acute cardiogenic pulmonary edema who received NIPPV for treatment and weaning from NIPPV was attempted at the ED. Data were collected from the Ramathibodi Hospital database and emergency medical records.

The eligibility criteria were patients older than 18 years, a clinical diagnosis of acute respiratory failure caused by acute cardiogenic pulmonary edema based on ESC criteria, and the requirement of noninvasive ventilation and weaning from noninvasive ventilation at the ED. The exclusion criteria were use of noninvasive ventilation within the previous 24 hours, hospitalization due to trauma or having a history of surgery in facial/oral/trachea/laryngeal areas within the past one month, hemodynamic instability, inability to protect the airways, excessive secretion, lack of cooperation, inability to fit the mask, and receiving hemodialysis or peritoneal dialysis during treatment.

2.3. Data gathering and outcome measures

The variables for determining clinical scoring of successful weaning from noninvasive ventilation were recorded for all



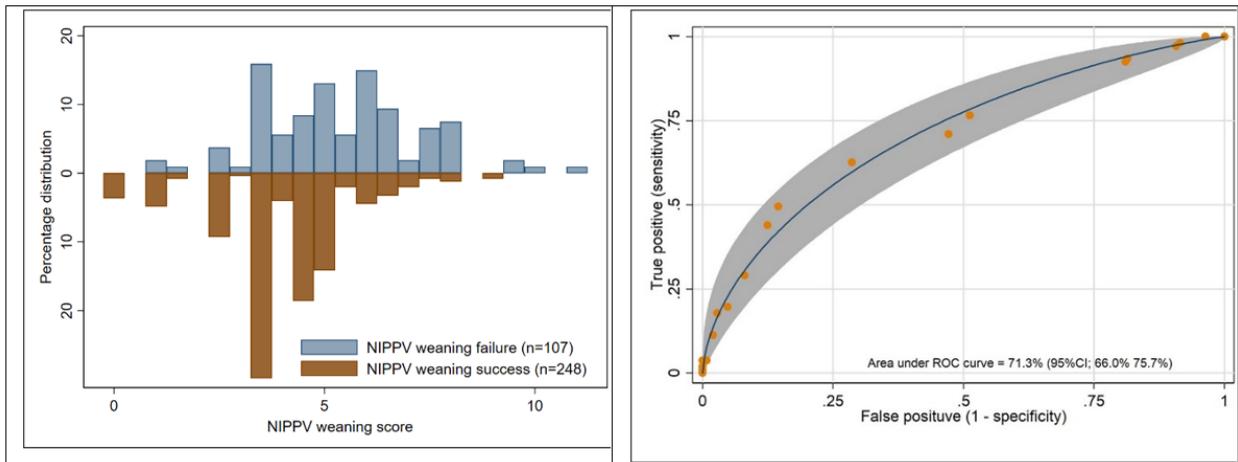


Figure 1: Left: Comparing the risk scores between patients with and without successful weaning from non-invasive positive pressure ventilation (NIPPV). Right: Area under the receiver operating characteristic (ROC) curve of model in predicting the risk of weaning failure from NIPPV in emergency department. Circle: The measures of calibration.

eligible patients, including baseline characteristics and potential clinical factors for successful weaning from noninvasive ventilation. Initial vital signs (respiratory rate, blood pressure, heart rate, body temperature, and SpO₂) were measured when the patient arrived at the triage zone of the ED. Vital signs before weaning were measured before deciding to discontinue NIPPV for the patient.

Laboratory variables (white blood cell count, hemoglobin, hematocrit, creatinine, blood urea nitrogen, sodium, potassium, and pro B-type natriuretic peptide (Pro-BNP)) were measured within 30 mins after the patient arrived at the ED. The first troponin blood test was collected 30 minutes after the patient arrived at the ED, and the second test was collected 3 hours later. The arterial blood gases (pH, PaO₂, PaCO₂, HCO₃, lactate, oxygen saturation) were measured before the patient applied NIPPV and within 90 minutes before discontinuing NIPPV. The door to NIPPV was recorded as the time interval between when the patient arrived at the ED and when NIPPV was applied. The duration of NIPPV was the total time the patient was using NIPPV in ED.

The setting of NIPPV (mode of NIPPV, inspiratory pressure, expiratory pressure, pressure support, positive end-expiratory pressure (PEEP), FiO₂) was recorded when the emergency resident or emergency physician initiated and before weaning of NIPPV. The diuretic dose was the accumulated dose of furosemide that the patient was given while receiving NIPPV. The urinary output was the total amount of urine during the period the patient received NIPPV. The cardiologist or emergency physician measured the ejection fraction (EF) during the period the patient received NIPPV.

2.4. Definitions

Weaning success: After discontinuing NIPPV, the patient wasn't decided to reinitiate bilevel positive airway pressure (BIPAP) or undergo endotracheal intubation within 24 hours.

Weaning failure: After stopping NIPPV, the patient was decided to reinitiate BIPAP or undergo endotracheal intubation within 24 hours.

2.5. Statistical analysis

Twenty-eight (77.8%) patients had successful weaning from NIPPV, and eight (22.2%) patients had weaning failure, based on our pilot study. The ratio of success to failure to wean from NIPPV was 2.5:1.

STATA software version 14.0 was used to calculate the required sample size by using a two-sample comparison of success and failure to wean from NIPPV. The assumptions were as follows: alpha = 0.05 (two-sided test), the power of the sample size = 0.8, the ratio of the sample size = 2.5:1 and the level of statistical significance was < 0.05. The minimum number of patients required to determine statistical significance for each variable was calculated. A sample size of 247 was required for patients in the NIPPV weaning success group, and a sample size of 99 was required for patients in the NIPPV weaning failure group.

Data were analyzed using STATA version 14.0. The findings are presented as mean standard deviation, frequency (%), or median (inter quartile range). All study variables were compared between the NIPPV weaning success group and the NIPPV weaning failure group using the exact probability test for categorical variables and the t-test for continuous variables. The predictive power of each variable was calculated using univariate logistic regression and presented as the area



Table 1: Comparing the baseline characteristics of participants between cases with and without successful weaning from non-invasive positive pressure ventilation (NIPPV)

Characters	Successful (248)	Unsuccessful (107)	P value
Age (years)			
Mean \pm SD	75.1 \pm 12.5	78.1 \pm 11.1	0.011
< 60 years	35 (14.1)	6 (5.6)	0.017
60-75 years	67 (27.0)	23 (21.5)	
> 75 years	146 (58.9)	78 (72.9)	
Gender			
Male	92 (37.1)	28 (26.2)	0.051
Underlying disease			
Asthma/COPD	25 (10.1)	14 (13.1)	0.460
Bronchiectasis	5 (2.0)	1 (0.9)	0.673
Congestive heart failure	70 (28.2)	31 (29.0)	0.898
Ischemic heart diseases	118 (47.6)	39 (26.5)	0.062
Valvular heart diseases	86 (34.7)	42 (39.3)	0.470
Chronic renal failure	119 (48.0)	48 (44.9)	0.643
Neoplasm	26 (10.5)	10 (9.4)	0.849
Diabetes mellitus	135 (54.4)	57 (53.3)	0.908
Hypertension	206 (83.1)	91 (85.1)	0.755
Initial vital signs			
Respiratory rate (/min)	28.8 \pm 5.9	29.3 \pm 7.4	0.480
Systolic blood pressure (mmHg)	156.4 \pm 34.4	148.2 \pm 32.2	0.036
Diastolic blood pressure (mmHg)	82.0 \pm 16.8	76.4 \pm 14.2	0.003
Heart rate (bpm)	93.8 \pm 22.6	94.7 \pm 22.1	0.739
Body temperature ($^{\circ}$ C)	36.9 \pm 0.7	37.1 \pm 0.9	0.013
SpO ₂ (%)	92.0 \pm 7.8	91.2 \pm 7.4	0.378
Vital signs before weaning			
Respiratory rate (/min)	21.8 \pm 2.2	22.5 \pm 2.8	0.023
RR > 26 breaths/min	9 (3.6)	9 (8.4)	0.056
Systolic blood pressure (mmHg)	139.6 \pm 24.0	139.4 \pm 23.5	0.936
Diastolic blood pressure (mmHg)	73.9 \pm 13.4	72.6 \pm 14.1	0.390
Heart rate (bpm)	80.3 \pm 17.0	84.0 \pm 18.1	0.065
Heart rate > 80 bpm	117 (47.2)	62 (57.9)	0.040
Body temperature ($^{\circ}$ C)	36.9 \pm 0.7	37.2 \pm 0.4	0.268
SpO ₂ (%)	98.8 \pm 1.7	98.4 \pm 2.1	0.054
SpO ₂ < 97%	28 (11.3)	19 (17.8)	0.072
Laboratory values			
White blood cell count (cell/mm ³)	8810.4 \pm 5397.5	9083.8 \pm 4426.0	0.645
Hemoglobin (g/dL)	10.8 \pm 2.4	10.4 \pm 2.1	0.073
Hematocrit (%)	32.8 \pm 7.5	32.7 \pm 6.2	0.165
Creatinine (mg/dL)	2.2 \pm 2.7	1.7 \pm 1.3	0.095
Blood urea nitrogen (mg/dL)	33.0 \pm 22.0	31.0 \pm 18.8	0.415
Sodium (mmol/L)	137.1 \pm 5.9	136.1 \pm 5.7	0.167
Potassium (mmol/L)	4.3 \pm 0.6	4.2 \pm 0.7	0.409
Pro-BNP (pg/ml)	5771 (2245 - 11408)	4774 (2339 - 12108)	0.819
Troponin change > 20% (0, 3 h)	37 (21.4)	8 (11.8)	0.099
NIPPV			
Door to NIPPV (h)	0 (0 - 1)	1 (0 - 2)	0.093
Duration of NIPPV (h)	6 (4 - 11)	8 (4 - 13)	0.248
Initial setting of NIPPV			
PSV (cmH ₂ O)	13.2 \pm 1.9	13.1 \pm 1.5	0.736
PEEP (cmH ₂ O)	6.7 \pm 0.8	6.7 \pm 0.8	0.706
FiO ₂	0.4 \pm 0.2	0.4 \pm 0.2	0.642
Setting of NIPPV before weaning			
BiPAP mode before NIPPV	165 (66.5)	80 (74.8)	0.135
PSV (cmH ₂ O)	12.4 \pm 2.3	12.3 \pm 2.4	0.582

Table 1: Comparing the baseline characteristics of participants between cases with and without successful weaning from non-invasive positive pressure ventilation (NIPPV)

Characters	Successful (248)	Unsuccessful (107)	P value
CPAP mode before NIPPV	69 (27.8)	26 (24.3)	0.517
PEEP (cmH ₂ O)	6.5 ± 1.1	6.5 ± 1.0	0.924
FiO ₂	0.4 ± 0.1	0.4 ± 0.1	0.189
Diuretic usage			
Dose of diuretic (mg)	80 (40 -120)	80 (40 -120)	0.295
Urinary output (ml)	1500 (1100 -2200)	1300 (800 - 2000)	0.041
Urinary output/h (ml/h)	236.5 (150 - 394)	165 (100 - 300)	0.001
Urinary output < 150 cc/h	57 (23.0)	50 (46.7)	<0.001
Ejection fraction			
≥ 50%	82 (38.1)	47 (48.0)	0.206
41-50%	54 (25.1)	24 (24.5)	
≤ 40%	79 (36.7)	27 (27.6)	
Functional class (NYHA)			
1	2 (0.8)	0 (0.0)	0.632
2	30 (12.1)	14 (13.1)	
3	130 (52.4)	50 (46.7)	
4	86 (34.7)	43 (40.2)	
Comorbidities			
Pneumonia	22 (8.9)	26 (24.3)	<0.001
Anemia	73 (29.4)	41 (38.3)	0.108
Volume overload	70 (28.2)	22 (20.6)	0.147
Tracheobronchitis	7 (2.8)	8 (7.5)	0.079
Asthma/COPD	12 (4.8)	10 (9.4)	0.148
Sepsis	17 (6.9)	15 (14.0)	0.042
Acute renal failure	50 (20.2)	24 (22.4)	0.670
Arterial blood gases before NIPPV			
Arterial pH	7.40 ± 0.09	7.41 ± 0.06	0.661
PaCO ₂ (mmHg)	37.6 ± 14.7	33.7 ± 7.4	0.369
PaO ₂ (mmHg)	104.0 ± 71.0	103.7 ± 58.1	0.989
HCO ₃ (mmol/L)	21.7 ± 5.3	22.8 ± 4.5	0.323
Lactate (mmol/L)	2.6 ± 2.1	2.3 ± 2.0	0.667
Arterial blood gases before weaning from NIPPV (≤ 90 min)			
Arterial pH	7.44 ± 0.0	7.41 ± 0.01	0.103
PaCO ₂ (mmHg)	40.5 ± 11.8	42.8 ± 12.0	0.562
PaO ₂ (mmHg)	116.1 ± 52.5	152.3 ± 99.4	0.133
HCO ₃ (mmol/L)	25.8 ± 5.8	26.2 ± 6.6	0.827
Lactate (mmol/L)	1.4 ± 1.0	1.5 ± 0.7	0.682

Data are presented as mean ± standard deviation (SD), frequency (%), and median (Inter quartile range).

SD: standard deviation, COPD: Chronic Obstructive Pulmonary Disease, bpm : beats per minute, RR: Respiratory rate, h: hours, Pro-BNP: Pro B-type natriuretic peptide, NIPPV: non- invasive positive pressure ventilation, BiPAP: Bi-level Positive Airway Pressure, PSV: Pressure support ventilation, CPAP: Continuous Positive Airway Pressure, PEEP: Positive End Expiratory Pressure, NYHA: New York Heart Association, PaCO₂: partial pressure of carbon dioxide, PaO₂: partial pressure of oxygen, FiO₂: fraction of inspired oxygen.

under the receiver operating characteristic (AUC) curve with 95% confidence intervals (CI).

The potential predictors were categorized into three levels based on multivariable logistic regression. The regression coefficients of each clinical predictor were divided by the smallest coefficient and rounded to the nearest 0 or 0.5. Discrimination in the prediction of successful weaning scores is shown by the area under the ROC curve and 95% CIs. The calibration of the prediction was determined using the Hosmer–Lemeshow goodness-of-fit test, and the number and

percentages in each group are presented as the positive likelihood ratio, 95% CIs, and P values.

3. Results

3.1. Baseline characteristics of studied cases

395 patients with acute cardiogenic pulmonary edema who were treated with NIPPV and had available information on weaning from NIPPV at the ED were studied. 40 patients were excluded (34 patients received hemodialysis or peritoneal



Table 2: Multivariable logistic regression analysis of risk factors associated with weaning failure of non-invasive positive pressure ventilation (NIPPV)

Predictors	OR	95% CI	P value	Coefficient*	Score
Age (year)					
< 60	1.00	Reference	-	-	0
60-75	2.04	0.70-5.93	0.189	1.11	2.5
> 75	3.10	1.15-8.33	0.025	1.56	3.5
Pneumonia					
No	1.00	Reference	-	-	0
Yes	2.72	1.39-5.31	0.003	0.93	2
RR > 26 breaths/min					
No	1.00	Reference	-	-	0
Yes	2.65	0.91-7.73	0.075	1.45	3
HR > 80 bpm					
No	1.00	Reference	-	-	0
Yes	1.74	1.04-2.91	0.033	0.46	1
O2 saturation < 97%					
No	1.00	Reference	-	-	0
Yes	1.88	0.94-3.76	0.073	0.66	1.5
Urinary output < 150 cc/h					
No	1.00	Reference	-	-	0
Yes	2.93	1.74-4.91	< 0.001	0.77	1.5

Coefficients were obtained from multivariable binary logistic regression. The lowest coefficient obtained using multivariable logistic regression was 0.46, and the scores were split into groups of 0.5 points for each risk factor. OR: odds ratio; CI: confidence interval; Reference: reference category. RR: Respiratory rate, HR: Heart rate.

dialysis during NIPPV, 6 patients had used NIPPV within the previous 24 hours). Finally, 355 patients were enrolled, (248 (69.85%) patients were successfully weaned off NIPPV, and 107 (30.14%) patients were not successfully weaned (intubation or re-use of NIPPV within 24 hours). Table 1 compares the patients' baseline characteristics between cases with successful and unsuccessful weaning from NIPPV in ED.

Older patients had a significantly higher rate of NIPPV weaning failure than younger patients ($p = 0.017$). There was no statistically significant correlation between NIPPV success or failure and underlying diseases, laboratory results collected 30 minutes after the patient arrived at EDs, the initial setting of NIPPV, setting of NIPPV before weaning, ejection fraction, functional class (New York Heart Association; NYHA), arterial blood gases before NIPPV and before weaning from NIPPV.

The comorbidity of pneumonia, and sepsis was associated with a significantly higher incident of weaning failure ($p < 0.001$, and $p = 0.042$, respectively). Patients with a heart rate > 80 beats per minute and a respiratory rate > 26 breaths/minutes before weaning from NIPPV had a successful NIPPV weaning rate of 47.2% ($p = 0.040$) and 3.6% ($p = 0.056$), respectively. The urine output during the period of NIPPV < 150 cc/hours had a higher incidence in the weaning failure group (46.7% vs. 23%, $p < 0.001$).

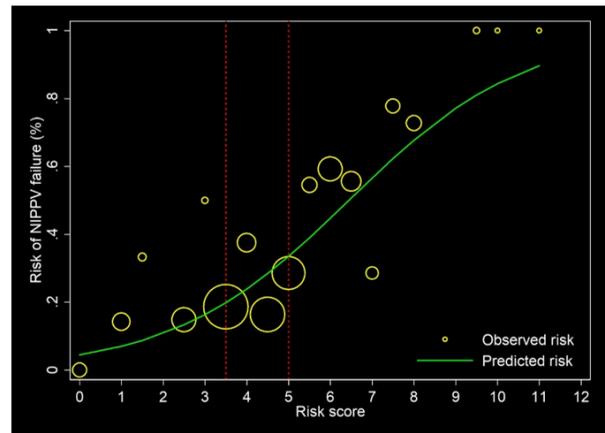


Figure 2: Comparing observed and predicted risks of failure to weaning from non-invasive pressure ventilation (NIPPV) in the studied cases.

3.2. Multivariable logistic regression analysis

In multivariable logistic regression analysis (Table 2), the statistically significant risk factors ($p < 0.05$) of weaning failure were patients older than 75 years (odds ratio [OR]: 3.1, 95% CI: 1.15–8.33, $p = 0.025$), pneumonia (OR: 2.72, 95% CI: 1.39–5.31, $p = 0.03$), pulse rate > 80 bpm before NIPPV (OR: 1.74, 95% CI: 1.04–2.91, $p = 0.033$), and a urinary output < 150 cc/h while using NIPPV (OR: 2.93, 95% CI: 1.74–4.91, $p < 0.001$).

Table 3: Probability categories of the non-invasive positive pressure ventilation (NIPPV) weaning failure score

Probability	Score	NIPPV weaning		LR+	95% CI	P value
		Failure (107)	Success (248)			
Low	≤ 3.5	25 (23.36)	121 (48.79)	0.48	0.33-0.69	< 0.001
Moderate	4-5	29 (27.10)	91 (36.69)	0.74	0.52-1.05	0.080
High	> 5	53 (49.53)	36 (14.52)	3.41	2.39-4.88	< 0.001

LR+: positive likelihood ratio; CI: confidence interval.

In addition, clinically significant risk factors for failure of weaning from NIPPV were age 60 – 75 years, respiratory rate > 26 breaths/min before weaning, and oxygen saturation of < 97% as assessed by pulse oximetry before weaning from NIPPV.

3.3. Designing a predictive model

The lowest coefficient obtained using multivariable logistic regression was 0.46, and the scores were split into groups of 0.5 points for each risk factor. As a result, patients aged < 60 years had no points, those aged 60–75 years had 2.5 points, and those aged > 75 years had 3.5 points. Patients with pneumonia had 2 points, those with a respiratory rate > 26 breaths/min before NIPPV had 3 points, those with a pulse rate > 80 bpm before NIPPV had 1 point, and those with an oxygen saturation by pulse oximetry < 97% had 1.5 points, and those with a urinary output < 150 cc/h while using NIPPV had 1.5 points (Table 2). The mean score of patients with unsuccessful weaning from NIPPV were significantly higher (5.37 ± 1.87 vs. 4.0 ± 1.63 ; $p < 0.001$). Figure 1(Left) compares the risk scores between cases with and without successful weaning from NIPPV.

To create the model, the failure to weaning risk score from NIPPV was assessed for each patient and the area under the ROC curve was 71.3% (95% CI: 66.0–75.7%) Figure 1(Right). Based on the area under the ROC curve, the cut point of risk score was divided into three categories (Table 3). The low-risk group had a positive likelihood ratio of 0.48 (95% CI 0.33–0.69, $P < 0.001$), the moderate-risk group had a positive likelihood ratio of 0.74 (95%CI 0.52–1.05, $P = 0.080$), and the high-risk group had a positive likelihood ratio of 3.41 (95%CI 2.39–4.88, $P < 0.001$) for weaning failure (Table 3). Figure 2 compares the observed and predicted risk of failure to wean from non-invasive pressure ventilation in the studied cases.

4. Discussion

Although NIPPV is the first-line treatment for acute respiratory distress induced by acute cardiogenic pulmonary edema, evidence and the treatment protocol for this condition are still insufficient. In this study, multivariate analysis showed that the likelihood of failure in weaning from NIPPV among patients with acute cardiogenic pulmonary signifi-

cantly increased in those aged > 75 years, those with pneumonia, those with a heart rate > 80 bpm before weaning, and those with a urinary output < 150 cc/h during NIPPV use. Other clinically significant risk factors for failure in weaning from NIPPV were age 60 – 75 years, respiratory rate > 26 breaths/min before weaning, and oxygen saturation of < 97% as assessed by pulse oximetry before weaning from NIPPV.

Based on the Framingham heart study, which reports the average annual incidence of acute cardiogenic pulmonary edema, we used the cut point of age at more than 60 years (13). We used the cut point of the respiratory rate at 26 bpm based on the recommendations for the initial treatment of acute heart failure with NIPPV in patients with respiratory distress (RR >25 breaths/min and SpO₂ < 90%) (14). Tachycardia was associated with failure to wean from NIPPV (15)(2). A 20% increase in cardiac troponin led to the diagnosis of acute myocardial infarction that may precipitate worsening symptoms of acute heart failure (16). Furthermore, regarding the urinary output, we used the recommendation of European Society of Cardiology 2022 that the appropriate management of diuretic therapy in a patient with acute heart failure was to monitor the urine output of more than 150 cc/h (14).

We also found that when patients undergoing NIPPV weaning were assessed using a risk score, a score of ≤ 5 (low or medium risk) enhanced their probability of successful weaning from NIPPV. Low-risk patients had a 0.48 likelihood of failing to wean from NIPPV. This group of patients reacted favorably to therapy.

This finding suggests that, in patients with acute cardiogenic pulmonary edema who present to the ED for risk score evaluation, NIPPV can be discontinued to decrease the risk of NIPPV complications and to alleviate overcrowding in EDs, which must cater to a high volume of critically ill patients.

Moderate-risk patients had a 0.74 likelihood of failing to wean from NIPPV. While risk ratings were predictive of successful weaning from NIPPV in this group of patients, the differences were not significant. As a result, when treating this group of individuals, if resources are not required for other critically ill patients, NIPPV should be continued until the patient's overall risk factor score shifts to a low-risk score. At this point, NIPPV should be discontinued. However, resources are constrained if there are constraints such as overcrowding



in the ED. Weaning from NIPPV and continuing to evaluate the prognosis of the disease closely in the ED is essential. If there is a likelihood that a patient cannot be weaned successfully from NIPPV, NIPPV must be restarted.

Patients at high risk had a 3.41 times greater likelihood of failing to wean off NIPPV. In this situation, NIPPV treatment should be continued until the patient's total risk score falls to moderate or low. Weaning from NIPPV should then be considered with close follow-up.

This study showed that increasing age increased the risk of weaning failure of NIPPV, particularly in patients aged > 75 and 60–75. No studies had shown evidence of an age-related risk factor for weaning failure. Therefore, risk factors for failure of weaning from NIPPV require further investigation.

Felker et al. studied the amount of diuretic administered to patients and found no effect on acute cardiogenic pulmonary edema therapy (17). In our study, the amount of diuretic used was the same in the NIPPV weaning success and failure groups. This finding is because the primary factor affecting patients' dyspnea and the effectiveness of weaning from NIPPV was the volume of urine produced by the patients, not the amount of diuretic administered. In this study, the most significant risk factor for weaning failure of NIPPV was a urinary output < 150 cc/h during NIPPV.

Acute cardiogenic pulmonary edema is caused by an accumulation of fluid in the alveoli and interstitial space (9). If a patient has a urinary output < 150 cc/h in the first 6 hours, diuretics and urinary output are increased to minimize the amount of volume overload. This is consistent with current heart failure therapy guidelines. This study showed that patients with a heart rate > 80 bpm before initiating weaning from NIPPV were more likely to have weaning failure. This finding is because cardiac dysfunction is the source of acute cardiogenic pulmonary edema (1). As a result, an increased heart rate may cause aberrant cardiac function (15). Additionally, there is evidence that the presence of pneumonia leads to the failure of weaning from NIPPV because pneumonia impairs the correction of desaturation (19). This is particularly challenging in individuals who have acute cardiogenic pulmonary disease.

No arterial blood gas risk indicators for weaning failure of NIPPV were identified in this study. Other studies have shown that decreased acidosis enhanced the success rate of NIPPV (15, 20, 21). When dyspnea is decreased, the majority of patients respond to therapy.

Additionally, this study's sample size may have been insufficient, which could have resulted in not finding a significant difference.

Momii et al. recommended a protocol for weaning, which included gradually modifying the ventilator mode and decreasing positive pressure every 30 minutes. The median duration of NIPPV was 8 hours, and the interquartile range was 0,

which improved the success rate in weaning from NIPPV (22). Positive pressure reduction data were not collected during NIPPV use in our study. There was no procedure for weaning from NIPPV, and the time to ventilator use or the ventilator mode (BIPAP or continuous positive airway pressure (CPAP)) before opting to wean from NIPPV was not associated with the incidence of weaning failure from NIPPV.

5. Limitations

This study has some limitations. This study was conducted at a university-affiliated super tertiary care hospital in Bangkok. Therefore, the patients' baseline prognostic factors may differ from those at other institutions. Additionally, weaning from NIPPV was required in the ED owing to restricted resources. Before applying these findings to a different situation, other hospital risk ratings (external validation) should be evaluated to determine whether predictive scores are reliable in predicting weaning from NIPPV in patients with acute cardiogenic pulmonary edema. Furthermore, this was a retrospective study. Some data were missing or incomplete, which resulted in incomplete data collection.

6. Conclusion

In patients with acute cardiogenic pulmonary edema under the NIPPV, weaning is associated with a significantly increased risk of failure in ages >75, presence of pneumonia, heart rate > 80 bpm before weaning, and urinary output < 150 cc/h during ventilation. Based on the model designed in this study, patients with score ≤ 3.5 points, 4–5 points, and > 5 had low, moderate, and severe risk of weaning failure, respectively. Weaning of high-risk patients should be postponed until their clinical prediction score shows a moderate or low risk or they should be closely observed after weaning.

7. Declarations

7.1. Acknowledgments

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7.2. Authors' contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.



7.3. Ethical considerations

This study was approved by the Faculty of Medicine, Committee on Human Rights Related to Research Involving Human Subjects, Ramathibodi Hospital, Mahidol University (COA. NO MURA2020/972). The ethics committee waived obtaining consent for this research as the patients' medical records were used for data gathering and a statement covering patient data confidentiality and compliance with the Declaration of Helsinki was provided.

7.4. Availability of data and material

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

7.5. Funding Source

No funding was obtained for this study.

7.6. Competing interests

The authors declare that they have no competing interests.

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