

HACOR Score as a Predictor of Non-Invasive Ventilation Failure Leading to Invasive Mechanical Ventilation and Mortality in Acute Respiratory Failure: A Prospective Study

Abegail Marie S. Yangyang, MD,¹ and Merci Angelie Letigio-Uy, MD¹

Abstract. It is critical to identify the parameters that can help predict patients with acute respiratory failure (ARF) who will fail on non-invasive ventilation (NIV), because delayed intubation following NIV failure shows a significant increase in in-hospital mortality. A reliable clinical tool that effectively identifies patients at risk for NIV failure is essential for timely intubation when it is imperative. This study aims to evaluate HACOR score in predicting NIV failure leading to invasive mechanical ventilation and/or mortality among patients with ARF who were admitted to a tertiary hospital in Cebu City from January 2022 to August 2022.

Methods. This prospective, observational, single-center study included adult patients admitted between January 2022 to August 2022 who were diagnosed with ARF type 1 and/or 2 and who were hooked to NIV as oxygen supplementation. Parameters of HACOR were collected and analyzed prior to initiation and 1 hour after hooking to NIV.

Results. Fifty adult patients with type 1 and/or type 2 ARF who required NIV were included. At 1 hour of NIV, the area under the receiver operating characteristic curve for the prediction of NIV failure, intubation, and mortality were 0.86, 0.89, and 0.80, respectively. Cut-off value for HACOR score was >5 with sensitivity in predicting NIV failure, intubation, and mortality, respectively: 78.3%, 82.4%, and 75%; the specificities were 92.6%, 92.9%, and 83.3%, respectively. Positive and negative predictive values were 90% and 83.3%, respectively. The computed overall accuracy was 86% (95% CI, 73.26–94.18).

Conclusion. We found that the HACOR score can be used as a tool to effectively predict NIV failure in patients with ARF, with a higher score indicating a higher chance of NIV failure. Variables in the HACOR score, including a lower Glasgow Coma Scale score and a higher respiratory rate, were shown to be independent factors associated with the need for endotracheal intubation. In these high-risk patients, early intubation may reduce the risk of adverse outcomes.

Keywords. *Non-invasive ventilation, Acute respiratory failure, HACOR*

Introduction

Non-invasive ventilation (NIV) is the administration of positive pressure ventilation through a non-invasive interface such as a nasal mask or face mask. It is an effective and safe technique to improve gas exchange, increase minute ventilation, and significantly reduce the

work of breathing among patients with hypoxemic and/or hypercapnic respiratory failure.¹ In the absence of strong indication for emergent endotracheal intubation, a cautious trial of 1–2 hours of non-invasive continuous positive airway pressure may be warranted, as it could prevent invasive ventilation and its associated complications.²

Although NIV plays a vital role in reducing the need for intubation among patients with respiratory failure, studies showed that mortality also increases significantly

¹Department of Internal Medicine, Perpetual Succor Hospital, Cebu City, Philippines
Corresponding author: Abegail Marie S. Yangyang, MD
Email: abegailyang@gmail.com

in patients associated with delayed intubation after NIV failure. In a prospective cohort study conducted by Correa et al., predictors of NIV failure included age and APACHE II score. NIV failure in patients with acute respiratory failure (ARF) was associated with increased in-hospital mortality, intensive care unit, and hospital stay. Patients that failed were comparatively younger, recommending the need for a prudent selection of patients that will benefit from NIV and the need for close monitoring of the more severe patients during NIV trial.³

Hence, it is critical to identify the variables that can help predict patients who will fail on NIV as early as possible, in order to have adequate timing and prompt intubation when it is imperative.

In a study by Yoshida et al., patients who underwent endotracheal intubation had a significantly lower arterial pH. The study found that a respiratory rate of more than 25 breaths per minute after 1 hour of NIV, together with lower pH, were independent factors associated with the need for endotracheal intubation.⁴

Previous studies have reported individualized variables that can predict NIV failure, including disease severity, heart rate, respiratory rate, consciousness, and arterial blood pH.^{4,5} These factors can be useful to predict NIV failure; however, the predictive power is low when based only on a single variable. A combination of several parameters may increase predictive accuracy. Thus, Duan et al. proposed a bedside obtained scale for the prediction of NIV failure in hypoxemia due to several causes. The scoring system was named HACOR and comprised multiple variables, specifically, heart rate, acidosis, consciousness level, oxygenation, and respiratory rate. The highest possible score was 25 points. The result of the study demonstrated that at 1 hour of NIV, a HACOR score >5 as the cut-off value showed a good distinguishing power for NIV failure, with a diagnostic accuracy of 81.8%.⁶

The advent of non-invasive ventilation has greatly contributed to the prevention of complications related to invasive ventilation. Growing evidence, however, shows increased mortality associated with delayed intubation following NIV failure.³ To date, no gold-standard clinical-decision tool is available, even locally, to conveniently detect patients at risk for failure of NIV. Thus, a good bedside scoring system that will aid future clinicians in the assessment and prudent decision-making for timely endotracheal intubation is warranted. Data from this study will also help physicians identify variables that are potential risks for poor NIV outcome, allowing close monitoring and early recognition of patients who will likely fail following NIV treatment.

Research Question

Can the HACOR score be used as a predictor for NIV failure leading to invasive mechanical ventilation and/or mortality among adult patients with ARF admitted at Perpetual Succor Hospital?

General Objective

This study aims to evaluate the HACOR score in predicting non-invasive ventilation failure leading to invasive mechanical ventilation and/or mortality among adult patients with ARF who were admitted to a tertiary hospital in Cebu City from January 2022 to August 2022.

Specific Objectives

1. To know the socio-clinical profile of patients who had NIV failure leading to endotracheal intubation and/or mortality
2. To identify the co-morbidities of patients who had NIV failure leading to endotracheal intubation and/or mortality
3. To determine the bedside variables, including heart rate, acidosis, consciousness, oxygenation, and respiratory rate, used in HACOR score in determining NIV failure
4. To know the outcomes of patients initially treated with NIV rather than invasive mechanical ventilation
5. To assess the sensitivity, specificity, positive and negative predictive values, and overall accuracy of HACOR score in predicting NIV failure
6. To investigate the predictors/risk factors of NIV failure in patients with ARF

Scope and Limitation of the Study

This study was conducted among adult patients, admitted in Perpetual Succor Hospital from January 2022 to August 2022, who were diagnosed with ARF type 1 and/or type 2, determined by clinical assessment plus the result of arterial blood gas (ABG) showing hypoxemia and/or hypercapnia. This study was limited to patients who were initially placed on NIV. Patients who had prophylactic use of NIV after extubation, rescue use of NIV after extubation, and use of a high-flow nasal cannula before NIV were excluded. Furthermore, this study was focused on the use of the HACOR score-based five bedside parameters; thus, confounding variables including the severity of the underlying disease and the medical treatment for each patient were not taken into account.

Methods

Study Design and Setting

This was a prospective, observational, single-center study conducted in Perpetual Succor Hospital, Cebu City, from January 2022 to August 2022. The Institutional Ethics and Review Board (IERB) of the hospital granted ethics approval.

Study Population and Sampling Procedure

The study enrolled adult patients admitted to the emergency room, ward, or intensive care unit, with a

diagnosis of ARF type 1 and/or type 2, who were initiated on NIV within the study period. Given the limited population, the study employed a complete enumeration technique, including all eligible individuals who met the inclusion criteria in the analysis.

Inclusion Criteria

1. Adult patients 18 years old and above
2. COVID- and non-COVID-confirmed patients
3. Use of NIV as oxygen support
4. Patients diagnosed with ARF type 1 and/or type 2
5. Baseline ABG determination revealing ARF with respiratory acidosis PaCO₂ >45 mmHg, pH <7.35, and/or hypoxemia with PO₂ <60 mmHg.

Exclusion Criteria

1. Prophylactic use of NIV after extubation
2. Rescue use of NIV due to respiratory failure after extubation
3. Accidental extubation and use of NIV
4. Use of a high-flow nasal cannula before or after NIV

Data Collection

Letters for approval were submitted to the IERB of the hospital before the conduct of the study. Data collection was started after ethical approval was granted. Patients meeting the inclusion criteria were provided with informed consent, which were written in both English and Cebuano and were explained thoroughly to the patient. If the patient was illiterate or unable to read due to any circumstance, the consent was explained verbally in layman’s terms to both the patient and/or their legal guardian. Data collected from the patients’ charts were handled confidentially, reviewed, collated, and analyzed. The socio-demographic and clinical characteristics, vital signs, and outcomes of patients were recorded. Data collection included the patient’s demographic data (age and sex); co-morbidities and other underlying diseases; vital signs, specifically heart rate and respiratory rate; level of consciousness based on the Glasgow Coma Scale; and ABG determination, including the pH and PaO₂/Fio₂ ratio. All the parameters of the HACOR score were collected before initiation of NIV and after 1 hour of hooking to NIV. HACOR score based on the five variables and their assigned points were computed and tabulated. Sixty-one adult patients with ARF were initially identified in the study. Eleven patients were excluded due to incomplete data, including failure to collect ABG after 1 hour. Patients who received prophylactic NIV post extubation, prior high-flow nasal cannula use, and intubation before NIV were also excluded (Figure 1). A total of 50 patients were included in the study, and the HACOR score (Table 1) was calculated for each. NIV was managed and adjusted by attending consultants, resident physicians, and respiratory therapists. A full-face mask was used as the interface to connect the ventilator to the patient. Selection of the size of the mask was fitted to the patient’s facial type. The straps were kept as tight

as possible to avoid air leaks while maintaining comfort. Ventilator settings, including positive end-expiratory pressure, pressure support, and the fraction of inspired oxygen, were adjusted based on PaO₂ and PaCO₂ from ABG analysis, as well as the severity of the patient’s distress. Settings were gradually titrated to optimize dyspnea control or to ensure patient tolerance to NIV treatment. The devices were ventilators on continuous positive airway pressure mode (the most commonly utilized devices were Puritan Bennett 7200 and Dräger Savina 300).

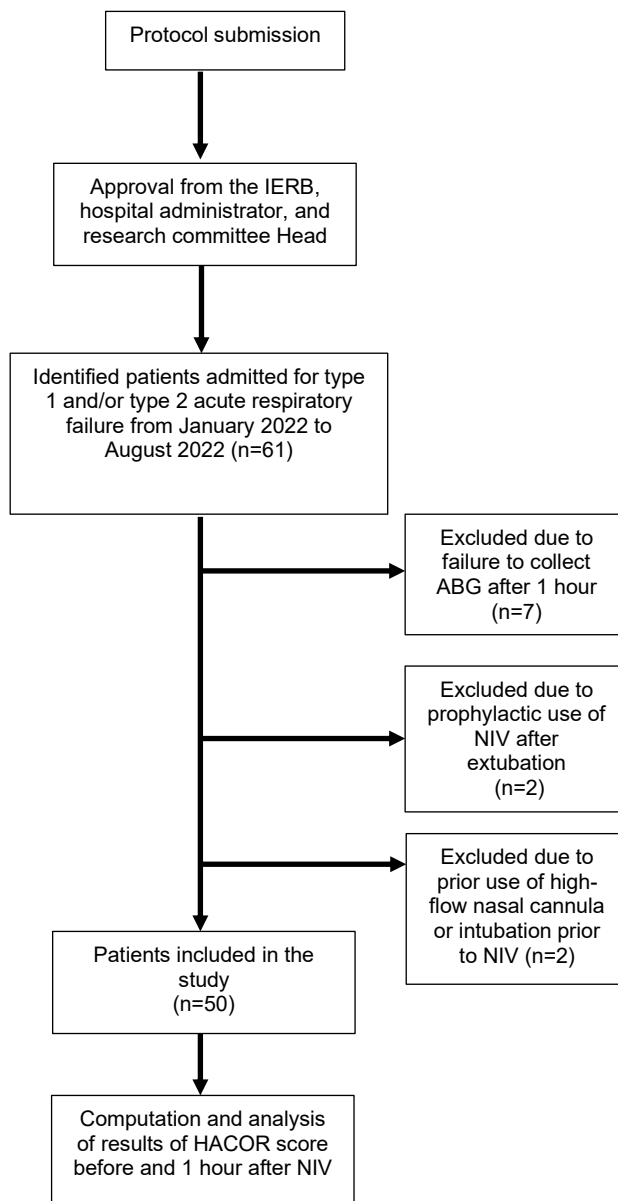


Figure 1: Data Collection and Analysis Workflow

Patients were followed up during the entire hospital stay. Their outcomes, including NIV success (defined as tolerance to NIV with successful weaning and absence of the need for subsequent invasive mechanical ventilation) and NIV failure (defined as intubation or death during NIV intervention) were recorded. NIV failure was based on the following criteria: cardiopulmonary arrest, severe

encephalopathy, severe gastrointestinal bleed, development of conditions necessitating intubation to protect the airway (coma or seizure disorders), inability to clear secretions, high-risk aspiration, inability to correct dyspnea, lack of improvement of signs of respiratory muscle fatigue, and hemodynamic instability without response to fluids and vasoactive agents.

The HACOR score was determined before and after 1 hour of NIV, and each parameter, including heart rate, arterial blood pH, Glasgow Coma Scale (GCS), PaO₂/FiO₂, and the respiratory rate, had corresponding points based on the original study by Duan et al. (Table 1). Heart rate ≤120 and ≥121 beats per minute were given 0 and 1 point, respectively. Acidosis was assessed by pH. pH ≥7.35, 7.30-7.34, 7.25-7.29, and <7.25 were given 0, 2, 3, and 4 points, respectively. Consciousness was assessed using GCS. GCS scores of 15, 13-14, 11-12, and ≤10 were given 0, 2, 5, and 10 points respectively. Oxygenation was assessed with PaO₂/FiO₂. PaO₂/FiO₂ ≥201, 176-200, 151-175, 126-150, 101-125, and ≤100 were given 0, 2, 3, 4, 5, and 6 points, respectively. Respiratory rates ≤30, 31-35, 36-40, 41-45, and ≥46 breaths per minute were given 0, 1, 2, 3, and 4 points, respectively. Parameters including heart rate, GCS, and respiratory rate were assessed and recorded by nurses and residents. ABG collection was done in a timely manner, and arterial blood specimen was processed in the hospital's diagnostic laboratory, using a regularly calibrated machine and performed by a licensed medical technologist. HACOR score was the sum of the points for the five variables, with the highest possible score of 25 points. The accuracy of HACOR score was then computed, including its sensitivity, specificity, positive predictive value, and negative predictive value.

Respiratory rate, breaths/min	≤30	0
	31-35	0
pH	36-40	1
	41-45	2
	≤46	3
	<7.25	4

Statistical Analysis

Descriptive statistics such as mean and standard deviation were used to describe the distribution of patients in terms of different numerical baseline variables. Frequency distribution and percentage were used to determine the distribution of patients in terms of different categorical baseline variables. Categorical variables were analyzed using the chi-squared test. A t-test was used to determine the association between NIV failure and success. The ability to predict NIV failure was determined using the area under the receiver operating characteristic curve (AUC).

P<0.05 was considered to be statistically significant.

Univariate binary logistic regression was used to determine if the different variables associated with each patient had a significant effect in predicting NIV failure, leading to intubation and/or mortality.

For this study, SPSS v.22, a statistical software package, was used in the statistical computations and analysis of data. MedCalc was utilized to determine the overall accuracy of the HACOR score.

The following terms were operationally defined in this study:

1. **NIV** refers to the delivery of positive pressure ventilation through a non-invasive interface using a face mask.
2. **HACOR score** is a scoring system, comprising heart rate, acidosis, consciousness level, oxygenation, and respiratory rate, used for prediction of NIV failure among patients with type 1 and type 2 ARF
3. **ARF**
 - 3.1. **Type I** refers to hypoxemia with PO₂ <60 mmHg on ABG
 - 3.2. **Type II** refers to hypercapnia with pH <7.35 and PaCO₂ >45 mmHg on ABG
4. **NIV failure** is defined as intubation or death during NIV intervention
5. **NIV success** is defined as effective use of NIV, without significant distress and/or complications, allowing for successful weaning and discontinuation

Table 1: Parameters of HACOR score and its corresponding points

Variable	Category	Assigned points
Heart rate, beats/min	≤120	0
	≥121	1
pH	≥7.35	0
	7.30-7.34	2
	7.25-7.29	3
	<7.25	4
GCS	15	0
	13-14	2
	11-12	5
	≤10	10
PaO ₂ /FiO ₂	≥201	0
	176-200	2
	151-175	3
	126-150	4

Ethical Issues

Patients’ data were handled with the utmost confidentiality. All information collected from the study or during its course was not divulged to any individual or organization. Names of healthcare personnel involved with the patient and their personal information were not included in the final manuscript.

Results

From January 2022 to August 2022, a total of 50 adult patients diagnosed with type 1 and type 2 ARF who required NIV treatment during their hospital admission were included in the study. The main socio-demographic profile and clinical characteristics are shown in Table 2. The predominant group was female (n=31, 62%), and the mean age was 60.8 ± 16.69 years. More than two-thirds

were non-smokers (n=36, 72%) while former and current smokers comprised 28% combined. The main identified co-morbidities among admitted patients were hypertension (n=35, 70%), heart failure (n=21, 42%), chronic kidney disease (n=21, 42%), and malignancy (n=18, 36%). The most common admission diagnosis was pneumonia with 15 patients (30%) followed by sepsis with 6 patients (12%) and pulmonary edema composed of 5 patients (10%). Thirty-five patients (70%) had type 1 respiratory failure, while 20 patients (40%) had type 2 respiratory failure.

In total, 23 patients (46%) had NIV failure: 17 (34%) underwent endotracheal intubation, while 5 (10%) were appraised with intubation due to failure of NIV but signed do-not-intubate order. The overall in-hospital mortality rate was 40% (n=20; Table 2).

Table 2. Demographics of patients with non-invasive ventilation failure and success.

Results are presented as absolute value (percentage) or as mean ± standard deviation.

	All subjects (n=50)	NIV success	NIV failure	P-value
Age (years) mean ± SD	60.8 ± 16.69	63.63 ± 15.9	56.55 ± 17.2	0.056
Sex, n (%)				0.042*
Male	19 (38%)	14 (28%)	5 (10%)	
Female	31 (62%)	13 (26%)	18 (36%)	
Smoking status, n (%)				0.206
Never	36 (72%)	17 (34%)	19 (38%)	
Former	9 (18%)	10 (20%)	4 (8%)	
Active	5 (10%)			
Underlying disease, n (%)				
Hypertension	35 (70%)	22 (44%)	13 (26%)	0.070
Heart failure	21 (42%)	12 (24%)	9 (18%)	0.778
CKD	21 (42%)	17 (34%)	4 (8%)	0.002*
Malignancy	18 (36%)	5 (10%)	13 (26%)	0.008*
Diabetes mellitus	17 (34%)	12 (24%)	5 (10%)	0.136
COPD	7 (14%)	5 (10%)	2 (4%)	0.430
Bronchial asthma	1 (2%)	1 (2%)	0 (0%)	1.000
Obesity	4 (8%)	1 (2%)	3 (6%)	0.322
OSA	2 (4%)	1 (2%)	1 (2%)	1.000
CHD	1 (2%)	0 (0%)	1 (2%)	0.460
CVD	1 (2%)	1 (2%)	0 (0%)	1.000
Sepsis	6 (12%)	2 (4%)	4 (8%)	0.395
Pneumonia	15 (30%)	6 (12%)	9 (18%)	0.228
Pulmonary edema	5 (10%)	5 (10%)	0 (23%)	0.054
History of COVID-19	17 (34%)	11 (22%)	6 (12%)	0.372

Type of ARF					0.548
	Type 1	29 (58%)	15 (30%)	14 (28%)	
	Type 2	16 (32%)	6 (12%)	10 (20%)	
	Both Type 1 and Type 2	5 (10%)	4 (8%)	1 (2%)	
Outcome					
	NIV Failure	23 (46%)			
	Intubation	17 (34%)			
	Refused Intubation	5 (10%)			
	In-hospital Mortality	20 (40%)			

ARF, acute respiratory failure; CHD, congenital heart disease; CHF, congestive heart failure; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; CVD, cerebrovascular disease; NIV, non-invasive ventilation; OSA, obstructive sleep apnea. *p<0.05.

There was no significant relationship between patients with NIV success and NIV failure in terms of age, smoking status, and certain co-morbidities such as hypertension, heart failure, diabetes mellitus, and chronic obstructive pulmonary disease. However, there was a noted significant relationship in gender, with females having a 36% (p=0.042) NIV failure rate. As to the underlying condition, malignancy was observed to have a high NIV failure rate (26%, p=0.008), while chronic kidney disease had an inverse relationship, with more NIV success rate (34%, p=0.002) than those who were not diagnosed with CKD (Table 2).

HACOR at 1 Hour and Its Clinical Outcome

Table 3 shows the comparison between HACOR parameters prior to NIV initiation and 1 hour after starting NIV. The mean HACOR score at 1 hour after hooking to NIV was 4.6 ± 3.61 as compared to 6.82 ± 4.74 before NIV initiation. There was a significant improvement in the respiratory rate (p=0.003), GCS (p=0.000), PaO₂/FiO₂ (p=0.040), and overall HACOR score (p=0.031) at 1 hour of NIV as compared to the results before starting NIV.

Table 3. Comparison between HACOR parameters and score before initiation of NIV and 1 hour after starting NIV

Variables	Before NIV, mean ± SD	1 H after NIV, mean ± SD	P-value
Heart rate (bpm)	108.74 ± 23.62	101.06 ± 21.76	0.668
Respiratory rate (cpm)	30.18 ± 5.71	27.42 ± 6.78	0.003*
Glasgow Coma Scale	13.78 ± 2.06	14.24 ± 1.42	0.000*
pH (ABG)	7.28 ± 0.13	7.32 ± 0.10	0.606
PaO ₂ /FiO ₂	212.8 ± 113.82	266.98 ± 119.01	0.040*
HACOR score	6.82 ± 4.74	4.6 ± 3.61	0.031*

Table 4 shows that patients who later experienced NIV success had a lower heart rate (97.76 ± 16.27 vs. 106.0 ± 27.82) and lower respiratory rate (26.33 ± 5.54 vs. 29.05 ± 8.17), while they also had higher pH (7.34 ± 0.099), higher GCS (14.73 ± 0.69 vs. 13.5 ± 1.88) and higher PaO₂/FiO₂ (302.2 ± 89.68 vs. 214.15 ± 139.1) than those who had a failure of NIV. Using the cut-off value of >5, the HACOR score was much higher in patients who experienced NIV failure (8.10 ± 2.53) than in patients with successful NIV (2.27 ± 1.94) when it was measured at initiation and after 1 h of NIV.

Table 4: Comparison between HACOR parameters and score of patients who had NIV success and NIV failure after 1H of NIV

Variables	Before NIV, mean ± SD	1 H after NIV, mean ± SD	P-value
Heart rate (bpm)	108.74 ± 23.62	101.06 ± 21.76	0.668
Respiratory rate (cpm)	30.18 ± 5.71	27.42 ± 6.78	0.003*
Glasgow Coma Scale	13.78 ± 2.06	14.24 ± 1.42	0.000*
pH (ABG)	7.28 ± 0.13	7.32 ± 0.10	0.606
PaO ₂ /FiO ₂	212.8 ± 113.82	266.98 ± 119.01	0.040*
HACOR score	6.82 ± 4.74	4.6 ± 3.61	0.031*

ABG, arterial blood gas; bpm, beats per minute; cpm, cycles per minute; FiO₂, fraction of inspired oxygen; HACOR, heart rate, acidosis, consciousness, oxygenation and respiratory rate; NIV, non-invasive ventilation; PaO₂, partial pressure of arterial oxygen. *p<0.005.

Table 5: Univariate binary logistic regression for significant risk factors associated with NIV failure

Variables/Factors	P-value	Odds ratio	95% CI for odds ratio	
			Lower	Upper
Gender	0.033	3.88	1.116	13.473
Co-morbidities				
Malignancy	0.007	5.72	1.600	20.445
CKD	0.002	0.12	0.033	0.499
HACOR variable				
GCS	0.014	0.42	0.208	0.840
HACOR score	0.001	1.690	1.258	2.271

CI, confidence interval; CKD, chronic kidney disease; HACOR, heart rate, acidosis, consciousness, oxygenation, and respiratory rate; NIV, non-invasive ventilation.

*p<0.05.

Table 6. The predictive power of overall NIV failure, intubation, and mortality diagnosed by HACOR score assessed at 1H of NIV

	Cutoff point	AUC (95% CI)	SN (%)	SP (%)	PPV (%)	NPV (%)	Diagnostic accuracy (%)
NIV failure	>5	0.862	78.3	92.6	90.0	83.3	86.0
Intubation	>5	0.892	82.4	92.9	87.5	89.7	88.9
In-hospital mortality	>5	0.799	75.0	83.3	75.0	83.3	80.0

AUC, area under the curve of receiver operating characteristics; CI, confidence interval; HACOR, heart rate, acidosis, consciousness, oxygenation, and respiratory rate; NIV, non-invasive ventilation; NPV, negative predictive value; PPV, positive predictive value; SN, sensitivity; SP, specificity.

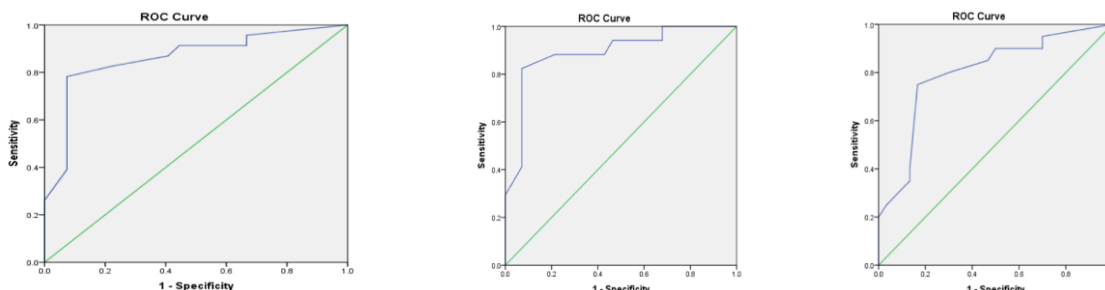
Factors Associated with Poor NIV Outcome

We found five risk factors associated with NIV failure in univariate analyses (Table 5). In comparison to gender, the odds of NIV failure were 3.9 times as much for female patients. The odds of NIV failure were 5.7 times as much for patients diagnosed with malignancy. Interestingly, NIV failure was 8 times as much for patients with no chronic kidney disease. Among the HACOR variables, NIV failure decreased by 87% for every unit increase in the GCS, while the odds of having NIV failure increased by 53% for every unit increase in the HACOR score.

HACOR Score and Its Overall Accuracy

At 1 hour of NIV, the AUC for the overall prediction of NIV failure, intubation, and mortality were 0.86, 0.89, and 0.80 respectively (Figure 2). After 1 hour of initiation to NIV, the cut-off value for HACOR score was >5 with the following sensitivities in terms of predicting NIV failure, intubation, and mortality: 78.3%, 82.4%, and 75%, respectively; conversely, the specificities of HACOR score in predicting NIV failure, intubation, and mortality were 92.6%, 92.9%, and 83.3%, respectively. The HACOR score had a positive predictive value in predicting NIV failure of 90% and a negative predictive value of 83.3%. The computed overall accuracy for the HACOR score in this population was 86% (95% CI, 73.26-94.18) (Table 6).

Figure 2. Receiver operating characteristic curves of the HACOR (heart rate, acidosis, consciousness, oxygenation, respiratory rate) score in predicting NIV failure (A), intubation (B), and mortality (C)



Discussion

HACOR Score and Its Overall Accuracy

NIV as a useful and safe treatment option for patients with ARF has reduced the odds of endotracheal intubation and mortality. However, several studies have shown that delayed intubation following untimely identification of NIV failure is subsequently associated with increased in-hospital mortality. Hence, there is a need for a scoring system that would help in predicting NIV failure following NIV use.

This study utilized a novel scoring system, the HACOR score, which was developed by Duan et al. This scale has five variables, including heart rate, acidosis, consciousness, oxygenation, and respiratory rate. The results of his study demonstrated that a HACOR score of 5 as the cut-off value had good distinguishing power for NIV failure. At 1 h of NIV, 87.1% of patients with a HACOR score >5 required endotracheal intubation, while 81.6% of patients with a HACOR score ≤5 did not. These results suggested that the risk of NIV failure was increased among patients with a HACOR score >5. Further, those high-risk patients who received early intubation had lower hospital mortality than those who received delayed intubation. Since the parameters in the HACOR score can be easily obtained using bedside measurements, this can be used as a potential tool to rapidly reassess patient's response to NIV treatment and to conveniently predict patients that would be at risk of NIV failure leading to endotracheal intubation and/or death.

The HACOR score was used in this study to predict the risk of NIV failure among admitted patients diagnosed with type 1 and/or type 2 ARF. In this study, the HACOR score had a good diagnostic accuracy of 86%, 88.9%, and 80% for predicting NIV failure, intubation, and mortality, respectively. At 1 h of NIV, the AUC for the overall prediction of NIV failure, intubation, and mortality were 0.86, 0.89, and 0.80 respectively. HACOR score also had a sensitivity of 78.3%, specificity of 92%, the positive predictive value of 90%, and a negative predictive value of 83.3%. The results of the study showed that HACOR score had high sensitivity and specificity for the prediction of NIV failure comparable to the original study by Duan et al.⁷

This study demonstrated that variables in the HACOR score, including a higher respiratory rate, similar to the study by Yoshida et al., were independent factors associated with the need for endotracheal intubation.⁴ Furthermore, a low GCS score together with a higher HACOR score of >5, proved to be associated with a higher NIV failure rate and higher mortality, consistent with the study by Duan et al.⁷ Among the co-morbidities, malignancy was an important independent risk factor for failure of NIV. Higher NIV failure and mortality rate among this subgroup could be attributed to the presence of metastasis, leading to multi-organ failure, poor performance status, and the decision to withhold treatment, including withholding intubation and cardiopulmonary resuscitation.^{6,8} Strikingly, NIV failure is eight times as much for patients with no chronic kidney

disease as compared to those who had been diagnosed with CKD. Among those patients with end stage renal disease on renal replacement therapy, prompt hemodialysis following NIV initiation contributed to good NIV outcomes in patients admitted for flash pulmonary edema.

Recommendation

Since the HACOR consists of parameters that are easily measured at bedside, it can be utilized efficiently to evaluate the efficacy of NIV and guide physicians in prompt clinical decision-making. We recommend doing a follow-up study on HACOR score in a multi-center trial with a larger population, encompassing wider array of conditions that result in ARF, to increase the precision of the findings and improve the diagnostic power. Second, future studies should consider conducting a subgroup analysis to assess the performance of HACOR score in different populations. This would help determine whether its predictive accuracy varies based on factors such as age, sex, underlying co-morbidities, and etiology of ARF. Third, we only observed and calculated the HACOR score before and 1 hour after NIV initiation. Therefore, our results cannot be fully compared with the original HACOR study, which included HACOR score assessments at 1, 12, 24, or 48 hours of NIV. The optimal timing for reassessment of HACOR score could be further investigated. Lastly, it would be interesting in the future to assess the efficacy of the HACOR score not only in predicting NIV failure but also in predicting failure rates of the high-flow nasal cannula and conventional oxygen therapy.

Conflict of Interest

The authors declare that there is no conflict of interest.

Funding

The authors received no financial support for the conduct and publication of this research.

References

1. TMeduri GU. Non-invasive positive-pressure ventilation in patients with acute respiratory failure. *Clin Chest Med.* 1996;17:513-553.
2. Franco C, et al. Feasibility and clinical impact of out-of-ICU non-invasive respiratory support in patients with COVID-19-related pneumonia. *Eur Respir J.* 2020;56:2002130.
3. Corrêa TD, et al. Performance of non-invasive ventilation in acute respiratory failure in critically ill patients: a prospective, observational, cohort study. *BMC Pulm Med.* 2015;15:144.
4. Yoshida Y, et al. Factors predicting successful non-invasive ventilation in acute lung injury. *J Anesth.* 2008;22:201-206.

5. Nicolini A, et al. Early non-invasive ventilation treatment for respiratory failure due to severe community-acquired pneumonia. *Minerva Pneumol.* 2019;58(1):1-6.
6. Basnet MB, Acharya KP, Adhikari D. Role of non-invasive mechanical ventilation for acute respiratory failure in cancer patients. *NMJ.* 2020;3(1):298-301.
7. Duan J, et al. Assessment of heart rate, acidosis, consciousness, oxygenation, and respiratory rate to predict non-invasive ventilation failure in hypoxemic patients. *Intensive Care Med.* 2017;43:192-199.
8. Azoulay E, et al. The prognosis of acute respiratory failure in critically ill cancer patients. *Medicine.* 2004;83(6):360-370.