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Using the HACOR Score to Predict Non-Invasive Ventilation Failure in Acute Hypoxemic Respiratory Failure

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Running Title: *HACOR score in predicting NIV failure*

Abstract: ***Acute hypoxemic respiratory failure (AHRF) is a leading cause of morbidity, and timely prediction of non-invasive ventilation (NIV) failure is crucial to prevent delays in escalation of care. This prospective observational study included 50 AHRF patients who received NIV and were classified after 48 hours as either success or failure based on clinical outcomes. The HACOR score—based on heart rate, pH, GCS, oxygenation, and respiratory rate—was assessed at initiation and after one hour. After one hour, the HACOR score significantly decreased in the success group and increased in the failure group. A HACOR score of 7 or more strongly predicted NIV failure, demonstrating high sensitivity (78.26%) and specificity (96.30%). The findings support the HACOR score as a reliable early indicator of NIV failure, enabling clinicians to make timely decisions that may reduce mortality.***

Keywords: Noninvasive Ventilation, Respiratory Failure, Hypoxemia, HACOR score

1. Introduction

Respiratory failure is the failure of optimal gas exchange. Acute hypoxemic respiratory failure (AHRF), the most common type, is defined by PaO_2 < 8 kPa or 60 mm Hg.[(1)] Mechanical ventilation is key to initial stabilization, reducing the work of breathing by creating an internal positive pressure milieu.[(2-5)] Invasive ventilation, using endotracheal or tracheostomy tubes, carries risks like ventilator-associated lung injury and pneumonia.[(6-8)] Non-invasive ventilation (NIV) avoids these but its failure raises mortality risk.[(9,10)] Factors like hypoxemia and altered consciousness lack predictive power for NIV failure.[(11-14)] Duan et al, using a combination of heart rate, blood pH, GCS, material oxygenation and respiratory rate, developed the HACOR score to address this.[(15)]

2. Materials and Methods

The study was a prospective observational study conducted in the department of Medicine, Lok Nayak Hospital.

Study population: Patients presenting with acute hypoxemic respiratory failure, initiated on NIV.

Inclusion criteria: Patients aged 18 years or more, with PaO2/FiO2 < 30 and preserved cough reflex.

Exclusion criteria: Patients with facial trauma, requirement of emergency intubation, depressed consciousness (Glasgow Coma Score < 12), unstable hemodynamic status, respiratory acidosis or hypercapnia and pregnant women.

Sample size:
Failure rate of NIV was reported as 47.8%, and the sensitivity of HACOR score to predict NIV failure in hypoxemic patients was 72.6% in the study by Duan et al.[(15)] So taking 10% margin of error, the sample size came out to be 165 patients. As this study is an exploratory effort, we took the sample size as 50 patients of acute hypoxemic respiratory failure requiring NIV.

Statistical analysis:
The collected data was analysed and statistically evaluated using SPSS-25 version. Quantitative data was expressed by mean, standard deviation or median with interquartile range and depending on normal distribution, difference between two groups was tested by student t test and Mann Whitney U test/ Kruskall Wallis test, and qualitative data was expressed in percentage and difference between the proportions was tested by chi square test and Fisher's exact test, wherever each was applicable. ROC curve was prepared using HACOR score to predict NIV failure in hypoxemic patients and cutoff value was calculated. p-value less than 0.05 was considered statistically significant. Correlation analysis of the data obtained of HACOR score and ROX index was done using Spearman rank correlation.

3. Methodology

The selected patients were tested for the variables like initial respiratory rate, initial PaO_2/FiO_2 ratio, HACOR score at presentation and at the end of 1 hour of initiation of NIV. Patients were observed for the next 48hours for the occurence of NIV failure, which was characterized by requirement of intubation, cardiorespiratory arrest, sustained PaO_2/ FiO_2 of <100, development of comatose state, excessive accessory respiratory muscle use and fatigue, and hemodynamic instability. The demographic profile, comorbid conditions, and clinical findings, as well as laboratory investigations which the patients underwent, like ABG analysis, complete blood count, liver, kidney and thyroid function tests, serum procalcitonin, pro-BNP and hsCRP levels, and other radiological and microbiological investigations, were noted. Complete patient confidentiality was maintained throughout the study and informed consent for participation taken from each participant. The study was reviewed and granted approval by the Institutional Ethics Committee (IEC), MAMC and associated hospitals, New Delhi.

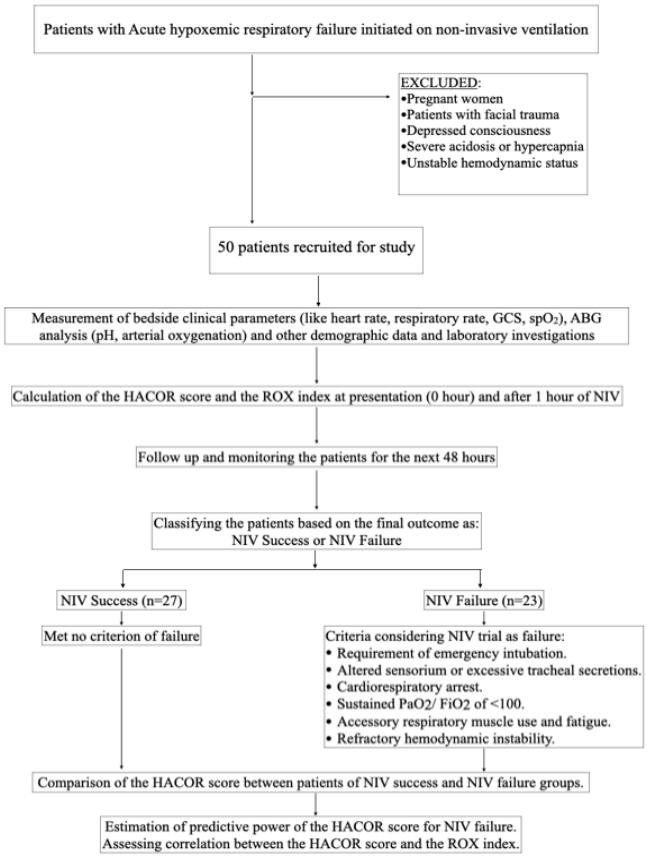

Figure 1: Outline of the Methodology of the study

4. Results

A total of 50 subjects who qualified the required criteria were included in the study. Of these 50, NIV failure was observed in 23 subjects (46%) and were categorised in the "NIV Failure" group. In the remaining 27 subjects (54%), NIV succeeded and they were classified into the "NIV Success" group. Subjects had a mean age of 42.74 years. The gender distribution was nearly balanced, with 52.0% of the participants being female. The mean body mass index (BMI) was 23.16 kg/m2.

Laboratory investigations

Many patients had elevated inflammatory markers such as procalcitonin (mean 6.01 ng/mL) and hsCRP (mean 5.9 mg/dL), which are commonly elevated in infections and inflammatory processes. The renal parameters, including elevated urea (mean 70.88 mg/dL) and creatinine (mean 2.43 mg/dL), suggest that renal dysfunction was common in this population.

Table 1: Distribution of various demographic, anthropometric, clinical and investigational parameters

Parameter			All Patients	Success Group	Failure Group	P-Value
Demographic parameters	Age (Years)	Mean (SD)	42.74 (14.53)	40.52 (15.66)	45.35 (12.93)	0.269
	Age Group	<30 Years	13 (26.0%)	9 (33.33%)	4 (17.39%)	0.016
		30 to 39 Years	5 (10.0%)	4 (14.81%)	1 (4.35%)	
		40 to 49 Years	14 (28.0%)	4 (14.81%)	10 (43.48%	
		≥50 Years	18 (36.0%)	10 (37.04%)	8 (34.78%)	
	Gender	Female	26 (52.0%)	14 (51.85%)	12 (52.17%)	0.982
		Male	24 (48.0%)	13 (48.15%)	11 (47.83%)	
Anthropometric parameters	BMI (kg/m2)	Mean (SD)	23.16 (4.5)	22.54 (4.22)	23.88 (4.79)	0.22
	Obesity	Underweight (<18.5 kg/m2)	8 (16.0%)	5 (18.52%)	3 (13.04%)	0.115
		Normal (18.5 – 22.9 kg/m2)	19 (38.0%)	12 (44.44%)	7 (30.43%)	
		Overweight (23 – 24.9 kg/m2)	4 (8.0%)	1 (3.7%)	3 (13.04%)	
		Obese (≥25 kg/m2)	19 (38.0%)	9 (33.33%)	10 (43.48%)	
Clinical findings	Heart Rate (Beats/Minute)	Mean (SD)	114.72 (23.15)	113.04 (24.36)	116.7 (22.03)	0.284
	Respiratory Rate (Breaths/Minute)	Mean (SD)	31.32 (4.29)	31.26 (4.16)	31.39 (4.53)	0.921
	spO2 (%)	Mean (SD)	63 (14)	66 (15)	60 (13)	0.098
	GCS	13	1 (2.0%)	1 (3.7%)	0 (0.0%)	< 0.001
		14	15 (30.0%)	6 (22.22%)	9 (39.13%)	
		15	34 (68.0%)	20 (74.07%)	14 (60.87%)	
	Systolic Blood Pressure (mm of Hg)	Mean (SD)	130.24 (23.29)	130.22 (23.73)	130.26 (23.29)	0.93
	Diastolic Blood Pressure (mm of Hg)	Mean (SD)	80.28 (15.62)	80.37 (15.94)	80.17 (15.60)	0.965
NIV related parameters	FiO2	Mean (SD)	72.22 (23.72)	62.63 (23.58)	83.48 (18.73)	0.002
Renal Parameters	Urea (mg/dL)	Mean (SD)	70.88 (68.82)	68.04 (66.80)	74.22 (72.49)	0.489
	Creatinine (mg/dL)	Mean (SD)	2.43 (2.93)	2.48 (2.88)	2.37 (3.06)	0.703
Other investigations	hsCRP (mg/dL)	Mean (SD)	5.9 (5.2)	5.73 (4.86)	6.10 (5.68)	0.838
	Procalcitonin (ng/mL)	Mean (SD)	6.01 (10.97)	7.23 (13.03)	4.57 (7.96)	0.546
	NT-ProBNP (pg/mL)	Mean (SD)	13004.9 (250027.07)	16639.67 (30057.72)	8738.0 (17090.35)	0.521

Risk factors, Co-morbidities and Etiologies:
A high prevalence of chronic conditions such as T2DM (32%), hypertension (24%) and CKD (24%) was noted among the participants as compared to the general population. A history of smoking and alcohol abuse was also noted in many subjects. A significant difference was found concerning type 2 diabetes mellitus, where 18.52% of the Success group were Type 2 diabetics, compared to almost half (47.83%) of the Failure group population. Pulmonary edema, present in 60% of patients, was the leading cause of respiratory failure, followed by pneumonia (40%).

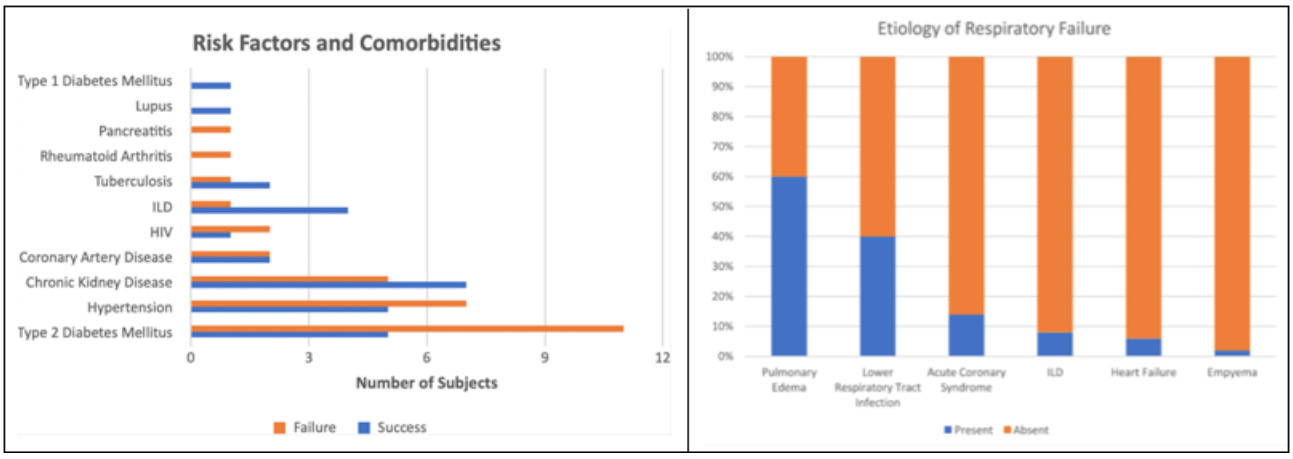

Figure 2: Distribution of the risk factors, co-morbidities and etiologies in the participants

Hemodynamic and Arterial blood gas parameters:
The respiratory rate (mean 32 breaths per minute) and heart rate (mean 114.72 bpm) were elevated in our subjects. Heart rate showed a statistically significant reduction in both groups after 1 hour of NIV, with a greater average reduction of 13.85 in the success group compared to the failure group with 8. Respiratory rate also significantly differed, decreasing more in the success group with a mean reduction of 10.37 breaths per minute compared to 2.7 in the failure group.

Arterial blood gas analysis confirmed the severity of respiratory distress, with a mean PaO_2 of 45.37 mmHg, consistent with the hypoxemia. NIV led to a notable improvement in the PaO2/FiO2 ratio in the success group, with a mean increase of about 50 compared to a mean

decrease of around 40 in the failure group. The spO_2 level improved substantially in both groups but was markedly higher in the success group. The ROX index, indicative of respiratory efficiency, also showed significant differences in the two outcome groups, with the decrease in the failure group (-5.28 ± 2.65) being more pronounced than the success group (-1.11 ± 2.71).

Table 2: Relation between the various parameters with NIV in AHRF among outcome groups

Change in parameter values (Value after 1 hour of NIV - Value Before NIV)		Outcome		P Value
		Success	Failure	
Heart Rate (Beats/Minute	Mean (SD)	-13.85 (16.49)	-8.0 (17.54)	0.014a
PaO_2/FiO_2	Mean (SD)	49.43 (74.46)	-41.27 (73.74)	<0.001a
Respiratory Rate (Breaths/Minute)	Mean (SD)	-10.37 (2.54)	-2.7 (5.48)	<0.001a

The HACOR score:

The HACOR score showed a significant trend after the use of NIV, where after 1 hour of NIV use, it dropped significantly in the success group from a mean of 3.26 to 1.52, Standard Deviation (SD)- 2.5, and increased in the failure group from 4.96 to 8.39 (SD 3.1). After the analysis of the data from all the participants, a score of 7 or above was strongly associated with NIV failure. There was also an inverse relation between the HACOR score and the ROX index.

Table 3: Relation between the HACOR score and the ROX index with NIV in AHRF among outcome groups

Parameter		Outcome		P Value
		Success (n=27)	Failure (n=23)	
HACOR Score – Before NIV	Mean (SD)	3.26 (2.96)	4.96 (3.31)	0.061a
HACOR Score – After NIV	Mean (SD)	1.52 (2.5)	8.39 (3.1)	<0.001a
ROX Index – Before NIV	Mean (SD)	10.32 (2.94)	9.58 (2.72)	0.364b
ROX Index – After NIV	Mean (SD)	9.21 (4.08)	4.3 (1.61)	<0.001a

5. Discussion

A logistic regression analysis was conducted to examine the relationship between NIV outcome and various predictors. Our results indicated that after one hour of NIV, PaO_2/FiO_2, respiratory rate and spO_2/FiO_2 were significant predictors of NIV failure.

Table 4: Univariate Logistic Regression for predicting Outcome

Independent Variable	Odds Ratio	Lower Bound of 95% CI	Upper Bound of 95% CI	P Value
Pao2/Fio2 – After NIV	0.988	0.98	0.995	0.001
Respiratory Rate – After NIV	1.496	1.215	1.842	<0.001
sPO2/FiO2 – After NIV	0.979	0.966	0.992	0.002

The relevant predictors were combined into a multivariate model showing that although the overall model was significant (Log Likelihood (11.0, 38.0) = 61.74, p value <0.001) and accounted for 89.49% of the variance in Outcome (Adjusted R^2 = 0.89), none of the individual predictors were significant after adjusting for other variables suggesting potential collinearity or interdependence among predictors.

Table 5: Multivariate Logistic Regression for predicting Outcome

Independent Variable	Odds Ratio	Lower Bound of 95% CI	Upper Bound of 95% CI	P Value
PaO_2/FiO_2 – After 1 hr of NIV	1.134	0.971	1.324	0.112
Respiratory Rate – After 1 hr of NIV	2.648	0.867	8.092	0.088
spO_2/FiO_2 – After 1 hr of NIV	0.729	0.444	1.196	0.21

The HACOR score serves as a reflective measure of the respiratory distress for the patient with consideration for important systemic factors. Before NIV use, although the average score was lower in the success group, 3.26, compared to the failure group, 4.96, the difference did not reach the limits of statistical significance. The use of NIV for 1 hour showed a significant reduction of the HACOR score in the success group, with a mean decrease of 1.74, while the failure group experienced worsening, with an increase of 3.43. This is consistent with the findings of the study by Duan et al, where after 1 hour of NIV, the average HACOR score of the success group decreased from 4.5 to 2.5, while it increased in the failure group from 7.5 to 7.9.

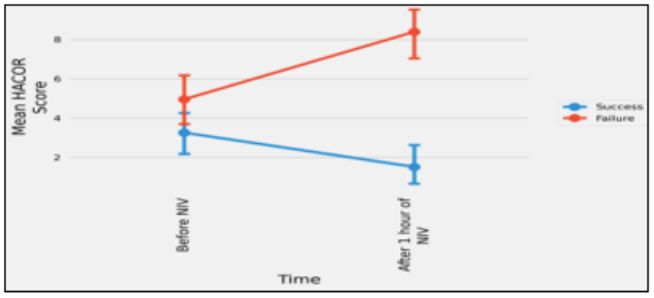

Figure 3: Trend of the HACOR score with NIV use in the two outcome groups.

A receiver operating characteristic (ROC) analysis was conducted to determine the optimal cutoff levels for the HACOR score to classify subjects based on their final NIV outcomes. The HACOR score at presentation before starting NIV had a modest utility for this purpose, as a score of ≥ 6 had a sensitivity, specificity, positive and negative predictive value (PPV and NPV) of 47.83%, 74.07%, 61.11% and 62.50%, respectively, with area under the ROC curve- 0.655; 95% CI 0.501-0.808 (overall accuracy 62%) (p- 0.049). Among the participants that succeeded the NIV trial, about three quarters (74.07%) of them had a HACOR score of less than 6 at the beginning of NIV. Also, of the 32 patients from the total cohort that had an initial HACOR score of less than 6, NIV success was seen in 84.37% of them.

After 1 hour of NIV, the discriminatory power of the HACOR Score in classifying subjects as NIV Failure was excellent (area under the ROC curve- 0.936; 95% CI 0.861 – 1.0). Except for one patient, all 27 patients that had success with NIV had a score of less than 7. From a total of 19 participants out of 50 that had a HACOR score of 7 or more after 1 hour of NIV, all but one participant failed the trial of NIV. Using a cut-off value of ≥7.0, the sensitivity was found to be 78.26% and the specificity was 96.30% and the Negative and Positive Predictive Values were 83.87% and 94.74%, respectively ($p<0.001$). The overall accuracy was 84.0%. These findings align with those reported by Duan et al with the HACOR score in their study at 1 hour of NIV use with a cut off value of ≥ 5, with sensitivity 73.9%, specificity 91.4%, PPV 87.1%, NPV 81.6% and accuracy of 83.7%.[15]

Table 6: Statistical characteristics of the HACOR score.

Predictor	AUC	95% CI of AUC	Sensitivity	Specificity	PPV	NPV	Accuracy	P Value
HACOR Score – Before NIV≥6.0	0.655	0.501-0.808	47.83%	74.07%	61.11%	62.50%	62.00%	0.049
HACOR Score – After 1 hr of NIV≥7.0	0.936	0.861-1.0	78.26%	96.30%	94.74%	83.87%	88.00%	<0.001

The observed improvement in the predictive power of the HACOR score after NIV shows that it can be used to assess the adequacy of the response to ventilatory therapy in patients with AHRF.

We found a significant negative correlation between HACOR scores and ROX indices across various time points, with a correlation coefficient -0.77 before NIV initiation, and -0.81 after one hour of NIV ($p < 0.001$). These findings suggest an inverse relationship between the HACOR score and the ROX indices.

Table 7: Relation of the HACOR score with the ROX index.

Parameter	Correlation Coefficient	P Value
HACOR Score – Before NIV versus ROX Index – Before NIV	-0.77a	<0.001
HACOR Score – After 1 hr of NIV versus ROX Index – After 1 hr of NIV	-0.81a	<0.001

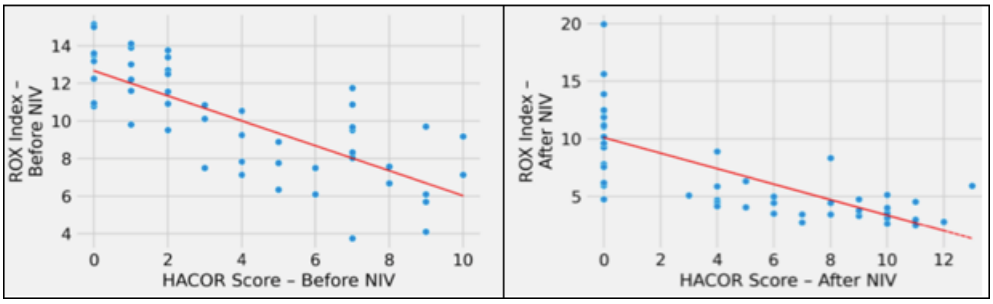

Figure 4: Scatter plots between the HACOR score – Before NIV and ROX index – Before NIV and between HACOR score after 1 hour of NIV and ROX index after 1 hour of NIV.

Non-invasive ventilation (NIV) is now widely employed as the first-line ventilatory support in patients presenting with acute hypoxemic respiratory failure (AHRF), especially in emergency departments and intensive care units (ICUs).[2] NIV offers several advantages over invasive mechanical ventilation (IMV), including reduced risk of ventilator-associated complications, such as ventilator-associated pneumonia, lung injury, and hemodynamic instability.[6–8] Furthermore, NIV is the standard of care for initial management of patients with hypercapnic respiratory failure.[2] However, in patients with AHRF, the failure of NIV is not uncommon and has been consistently associated with increased morbidity and mortality.[9,10]

When NIV fails, patients often require emergency endotracheal intubation and transition to IMV. Studies have shown that the timing of this transition plays a crucial role in patient outcomes. Specifically, early intubation following NIV failure is associated with improved survival rates compared to delayed intubation.[16] Thus, identifying patients at high risk of NIV failure early during the course of therapy is essential for optimizing outcomes and preventing deterioration.

Traditional clinical predictors such as hemodynamic instability, altered mental status, or severe hypoxemia have been associated with NIV failure but lack sufficient individual predictive power.[11–14] To address this limitation, Duan et al. developed the HACOR score, which incorporates heart rate, arterial pH, Glasgow Coma Scale (GCS), oxygenation (PaO_2/FiO_2), and respiratory rate—parameters that are readily measurable at the bedside.[15] This scoring system provides a composite measure that reflects the overall physiological burden and has shown strong predictive value for NIV failure.

In the present study, we observed that the HACOR score measured one hour after NIV initiation had excellent discriminative ability in predicting NIV failure, with a high area under the ROC curve and good sensitivity and specificity at the optimal cut-off. These findings support the practical utility of the HACOR score as a bedside tool to guide clinical decision-making. By identifying patients unlikely to benefit from ongoing NIV, clinicians can promptly escalate to invasive ventilation when indicated, potentially reducing the risks associated with delayed intervention.

Therefore, routine application of the HACOR score during the early phase of NIV could enhance patient stratification, improve timely intervention, and ultimately lead to better clinical outcomes in AHRF patients.

There are a number of limitations in our study. The study's relatively small sample size of 50 subjects might limit the generalisability of findings to a broader population of patients. The single-center design of the research potentially introduces a bias related to geographical and demographic factors. Since our study does not have a longitudinal follow up of all the patients, the data regarding the final outcome of the patients of AHRF who were initiated on NIV, in terms of mortality benefit, is not available in entirety.

6. Conclusion

The early prediction of non-invasive ventilation failure in patients with acute hypoxemic respiratory failure is of paramount importance to improve clinical outcomes. Our study demonstrates that the HACOR score, a simple bedside tool incorporating easily measurable clinical parameters, offers strong predictive value for identifying patients at risk of NIV failure, after one hour of therapy. Timely recognition of high-risk patients using the HACOR score can guide prompt escalation to invasive ventilation, potentially reducing mortality associated with delayed intubation. Incorporating the HACOR score into routine clinical practice may enhance decision-making and optimize management strategies for AHRF patients.

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