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Original Article

Acute Hemodynamic Index as a Predictor of In-Hospital Mortality in Mechanical Ventilated Acute Decompensated Heart Failure Patients

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ABSTRACT

Background: The likelihood of a poor clinical outcome is significantly increased in patients with acute decompensated heart failure. Mechanical ventilation was necessary for 23% of ADHF patients receiving treatment. The simple parameters of blood pressure and heart rate have good accuracy and repeatability. The development of the Acute Hemodynamic Index allowed for the calculation of pulse pressure and heart rate to be used as a basis for predicting intrahospital mortality.
Objectives: To understand the characteristics of AHI so that it could be applied as a predictor of in-hospital mortality in patients with acute decompensated heart failure with mechanical ventilation who were treated in the CVCU at Saiful Anwar General Hospital
Methods: The medical records of patients who received care at CVCU RSSA were used in this retrospective, single-center study. ROC analysis and multivariate regression analysis were used to evaluate the prognostic performance of AHI. Statistical significance was determined by the P value of 0.05 or lower.
Result: 252 patients with heart failure and low ejection fraction had their data analyzed. Hospital mortality is 82 percent. The cut-off was 4.19 mmHg/bpm, which was the AHI value. 68.8% of patients with fatal illnesses had low AHIs (4.19 mmHgbpm). AHI > 4.19 mmHgbpm patients have a 9-fold increased risk of dying in the hospital than patients with low AHI. AUC: 0.825 [0.743-0.907]; sensitivity: 0.814; specificity: 0.689; AUC: 0.825 [0.743-0.907; p = 0.000]; demonstrate the high predictive power of AHI.
Conclusion: AHI has a strong degree of association with the likelihood of dying in the hospital from acute decompensated heart failure.

1. Introduction

Heart failure (HF) is the leading cause of hospitalization, mortality, and a growing healthcare burden.[1] HF mortality rates range from 4% to 7% during hospitalization, from 7% to 11% at 60–90 days, and from 25% to 30% at 60–90 days after discharge. The AHEAD registry reports an in-hospital mortality rate as high as 53% among patients with acute heart failure who are mechanically ventilated.[2]

There is an urgent need for strategies to shorten hospital stays, prevent re-hospitalization, and provide appropriate care for each stage of heart failure given the high cost of inpatient heart failure treatment and the expanding number of population at risk.[3]

Any healthcare professional can easily obtain blood pressure (BP) and heart rate (HR) with good repeatability and accuracy. In the Framingham study, increasing the baseline pulse pressure (PP) line carries a significant risk for coronary artery disease and heart failure and, in some of the studied populations, independently predicted overall cardiovascular-related mortality. Additionally, a poor HR response to physiological stress may have negative effects.[4-6]

Acute Hemodynamic Index (AHI) calculations using HR and PP were proposed by Castro et al. as a standalone predictor of in-hospital mortality in acute decompensated HF (sensitivity: 0.786; specificity: 0.429; AUC: 0.607 [0.540–0.674]; p = 0.010).[7]

In this regard, the researchers conducted further studies to understand the characteristics of AHI so that it could be applied as a predictor of in-hospital mortality in patients with acute decompensated heart failure with mechanical ventilation who were treated in the CVCU at Saiful Anwar General Hospital.

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Table 1. Baseline Characteristics of Acute Decompensated Heart Failure Patients receiving Mechanical Ventilation in the dr. Saiful Anwar General Hospital, Malang

No	Variable	Discharged Patients (n= 43)	Deceased Patients (n=209)	P-Value
	Demographic			
1	Age (mean ± SD)	61.0 ± 14.3	61.1 ± 13.6	0.997
2	Sex (n, %)			0.555
	Male	23 (53.5%)	20 (46.5%)	
	Female	122 (58.4%)	87 (41.6%)	
3	BMI	24.6 ± 4.6	24.2 ± 4.6	0.560
	Etiology			0.621
1	Non-IMA (n, %)	22 (51.2%)	115 (55.3%)	
2	IMA (n, %)	21 (48.8%)	94 (44.7%)	
	Comorbidities			
1	Hypertension (n, %)	30 (69.8%)	88 (42.3%)	0.001
2	Diabetes Mellitus (n, %)	9 (20.9%)	54 (25.8%)	0.499
3	Smoker (n, %)	9 (20.9%)	51 (24.4%)	0.626
4	CKD (n, %)	0 (0%)	5 (2.4%)	0.306
5	Dyslipidemia (n, %)	16 (37.2%)	49 (23.4%)	0.060
6	Stroke (n, %)	1 (2.3%)	15 (7.2%)	0.235
7	Atrial Fibrilation (n, %)	2 (4.7%)	20 (9.6%)	0.298
	Treatment History			
1	ACEi/ARB (n, %)	13 (30.2%)	40 (19.1%)	0.104
2	Beta blocker (n, %)	6 (14.0%)	26 (12.5%)	0.795
3	Inotropic/Vasopressor (n, %)	16 (37.2%)	96 (46.2%)	0.283
4	CCB (n, %)	1 (2.3%)	2 (1.0%)	0.451
5	Spironolactone (n, %)	5 (11.9%)	18 (8.7%)	0.506
6	Statin (n, %)	10 (23.3%)	57 (27.3%)	0.587
7	Antiplatelet (n, %)	10 (23.3%)	56 (26.8%)	0.631
8	Anticoagulant (n, %)	7 (16.3%)	39 (18.7%)	0.713
9	Furosemide (n, %)	8 (18.6%)	36 (17.2%)	0.828
	Hemodynamic			
1	Heart Rate (bpm)	110 ±16	93 ± 21	0.000
2	Systolic Blood Pressure (mmHg)	132 ± 23	112 ± 22.9	0.000
3	Diastolic Blood Pressure (mmHg)	76 ± 20	73 ± 19	0.271
4	Pulse Pressure (mmHg)	55 ± 10	39 ± 11	0.000
5	Acute Hemodynamic Index (mmHg.bpm)	6.30 ± 2.28	3.89 ±1.41	0.000
6	P/F Ratio (%)	205 ±154	162 ± 102	0.021
7	EF (%)	33.1 ± 7.7	31.7±7.2	0.294
	Laboratorium			
1	Hb (g/dL)	12.2±2.7	12.4±2.7	0.656
2	Ht (%)	37.3±8.3	37.4±8.6	0.975
3	Kreatinin (mg/dL)	2.1±2.6	2.5±3.6	0.410
4	BUN (mEq/L)	18.0±10.3	18.7±9.7	0.694
5	Sodium (mEq/L)	138±3.9	135±5.8	0.002
6	Kalium (mEq/L)	3.8±0.67	4.1±1.0	0.008
7	pH	7.22±0.15	7.26±0.13	0.147
8	pO2 (mmHg)	133±67	118±62	0.200
9	pCO2 (mmHg)	44±24	40±22	0.398
10	HCO3 (mEq/L)	20.4±8.8	18.1±6.5	0.047
	Clinical Profile			
	Forrester			0.555
1	Dry Warm (n, %)	14 (32.6%)	43 (20.6%)	
2	Wet Warm (n, %)	13 (30.2%)	54 (25.8%)	
3	Dry cold (n, %)	9 (20.9%)	42 (20.1%)	
4	Wet Cold (n, %)	7 (16.3%)	70 (33.5%)	
	NYHA			0.006
1	Class I (n, %)	0	0	
2	Class II (n, %)	0	0	
3	Class III (n, %)	33 (78.6%)	117 (21.4%)	
4	Class IV (n, %)	9 (56.0%)	92 (44.0%)	

Our primary hypothesis was that AHI could serve as an objective in-hospital prognostic metric for patients with acute decompensated Heart Failure with reduced Ejection Fraction. Therefore, we assessed the prognostic value of AHI in hospitalized patients with acute decompensated HFrEF.

2. Material and Methods

2.1 Studi Design

This analysis is based on The Medical Record of Mechanical Ventilated Acute Decompensated Heart Failure (ADHF) patients in Saiful Anwar General Hospital Malang, a retrospective cohort, collected from January 2015 to December 2021. For inclusion criteria, patients should be over 18 years old and have been admitted with decompensated HF; patients should not have been admitted with a sepsis diagnosis. The participation did not require any special treatment regimen. This study analyzes patients with reduced ejection patients from the time they are admitted to the hospital until they are deceased or discharged. In-hospital mortality was the primary endpoint of the study. Patients with missing data were excluded from the current analysis (admission heart rate, blood pressure, ejection fraction, or loss of follow-up). Individuals with a pacemaker-controlled heart rhythm were also excluded because their heart rate was not expected to be autonomically controlled. Patients who were admitted from another hospital for more than 24 hours were also excluded, as were those with cancer or other terminal illnesses. The medical record provided information on heart rate and systolic and diastolic blood pressure at admission, which was utilized to calculate the following derived variables: AHI = (pulse pressure x heart rate) / 1000; pulse pressure = systolic blood pressure - diastolic blood pressure.

2.2 Statistical Analysis

Kolmogorov Smirnov test validated parametric statistics and data normality. Categorical variables were reported as proportions. Clinical and demographic data from deceased and living patients were compared using unpaired Student's t-tests or chi-squared tests. Significant two-sided p0.05.

All univariate variables with a P value of 0.05 or higher were multivariate analyzed. Regression analyses were performed after checking for linearity, multivariate normality, homoscedasticity, multicollinearity, and autocorrelation. Variables received ROC curves. Using AUC, ROC curves were compared (AUC). each variable's sensitivity and specificity. All statistical analyses and graphs were performed using SPSS® 22.0

3. Results

This study included all patients with acute decompensated heart failure admitted to RSUD dr. Saiful Anwar Malang's Emergency Department (IGD) between January 2015 - December 2021 and received mechanical ventilation. Purposive sampling was used to select the research sample, which was then adjusted for inclusion. 369 subjects with mechanical ventilation were sampled. The study excluded 116 subjects. 17 patients had a qSOFA septic diagnosis, 39 needed a temporary pacemaker, and 61 had incomplete data. This study included 252 participants. Medical record tracing and laboratory data retrieval was done in Saiful Anwar General Hospital, Malang.

The intrahospital mortality index for mechanically ventilated patients was 82% based on patient characteristics. We did not analyze the high mortality rate further. 43 males and 209 females were surveyed. The study population's mean age was 56.3 9.1 years, ranging from 22-90. Hypertension was the most common comorbidity, found in 118 (47%), with a P-Value of 0.001 and OR 0.32 (0.15 – 0.64) 95% CI. 114 subjects (45.4%) had decompensation trigger factor IMA. Patients who died had more comorbidities and lower mean heart rate, pulse pressure, TDS, and TDD. Other hemodynamic profiles, such as ejection fraction, did not differ between living and dying subjects (33.1 7.7% and 31.7 7.2). Dead patients have a P/F ratio of 162 102 mmHg, which is worse than living patients (P 0.02).

112 study subjects (44.6%) received inotropes and vasopressors from referring health facilities in the last 24 hours before admission. Next, we will sub-analyze inotropic and vasopressor effects on AHI.

In this study, 12.7% of patients took beta blockers before admission. We did not continue sub-analyzing beta blockers' effect on AHI because the value was so low. When looking at the Forrester classification clinical profiles, most of the patients who died had a wet-cold profile in 70 study subjects (27.8%), although there was no statistical difference compared to the other 3 categories. At admission, all patients were NYHA III based on functional classification. There was no NYHA I-II subjects found.

From the results of multivariate analysis obtained AHI, P/F ratio, pulse pressure, and heart rate as predictors of intrahospital mortality. AHI had an inverse relationship with mortality with OR 0.6 (95% CI = (0.506-0.860).

Table 2. Multivariate Analysis with Logistic Regression

Parameter	P value	OR (CI 95%)
P/F_ratio	0.007	0.995 (0.991-0,999)
Pulse Pressure	0.000	0.846 (0.794-0.900)
Heart rate	0.000	0.897 (0.859-0.936)
AHI	0.002	0.660 (0.506- 0.860)

Note. significant if the p-value is 0.05 or lower

Receiver Operating Curve (ROC) analysis was performed to determine the threshold value of AHI in predicting intra-hospital mortality with certain sensitivity and specificity. The ROC curve shows a fairly good diagnostic value of AHI for the outcome of intrahospital mortality where the curve line is far above the 50% diagonal imaginary line. The AUC value of 82.5% (Figure 1) indicates the diagnostic ability of AHI for intrahospital mortality which is in the strong category.

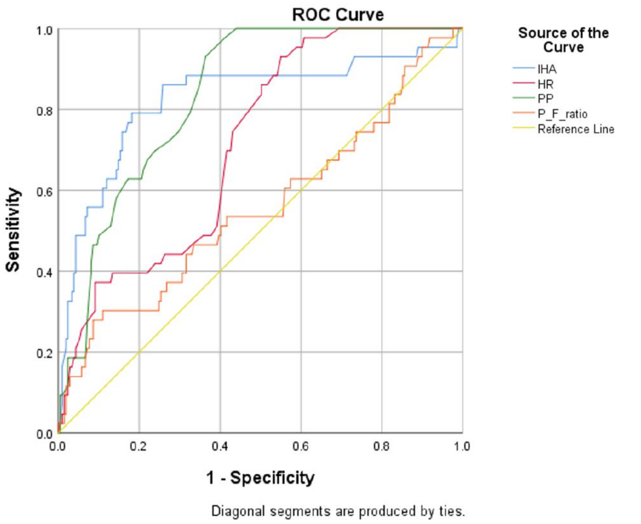

Figure 1. ROC curves of various variables on intrahospital mortality. AHI= Acute Hemodynamic Index; HR= Heart rate; PP: Pulse Pressure; P/F Ratio.

Table 3. Sensitivity, specificity, and AUC of various variables associated with intrahospital mortality

No.	Variable	Analysis ROC			
		Sensitivities	Specificities	AUC (95% CI)	P-Value
1	AHI	0.814	0.689	0.825 (0.743-0.907)	0.000
2	Heart rate	0.744	0.569	0.714 (0.639-0.788)	0.000
3	Pulse Pressure	0.791	0.675	0.836 (0.784-0.888)	0.000
4	P/F Ratio	0.535	0.584	0.555 (0.453-0.658)	0.253

Note. significant if the p-value is 0.05 or lower

From the ROC analysis, it is known that the threshold value <4.19 can be used to assess intrahospital mortality with a sensitivity of 86% and a specificity of 74%. In the results of $\chi 2$ based on the division of AHI <4.19 and > 4.19 groups, there were 208 subjects deceased and 43 subjects discharged. Of the 208 deceased subjects, 143 people (68.8%) of them had AHI < 4.19, while the remaining 65 people (31.3%) had AHI > 4.19. Of the 43 discharged subjects, 35 (81.4%) had AHI > 4.19 and 8 (18.6%) had AHI < 4.19.

Table 3. Relationship between inotropic/vasopressor administration and AHI

	Inotropik/Vasopressor		
	Tidak (n=139, 56%)	Ya (n=113, 44%)	p
AHI (mean ± SD)	**4.1 ± 1.5**	**4.5 ±2.0**	**0.136**

Note. significant if the p-value is 0.05 or lower

Inotropes and vasopressors have the potential to raise blood pressure and heart rate, which could have a direct impact on the AHI calculation, so we attempted to analyze the impact of their administration on AHI values.

According to the results of the T-test, the mean AHI increased by 4.5 ± 2.0 in subjects who received an inotropic/vasopressor but there was no statistically significant difference between the two groups (P=0.136). The average age of AHI for subjects who did not receive an inotropic/vasopressor was 4.1±1.5.

4. Discussion

The purpose of this study is to determine the predictive value of AHI in patients with acute decompensated heart failure receiving mechanical ventilation. Mortality within the hospital of patients with acute decompensated heart failure receiving mechanical ventilation. Dr. Saiful Anwar Malang demonstrates a greater value than that reported in the AHEAD registry, which is 82% and 53%, respectively.[2] Possible explanations for the disparity include age variation, comorbidities, and the delay between symptom onset and hospitalization. Because the management of patients with acute heart failure may involve complex and expensive procedures, it is essential to validate prognostic factors that can guide treatment decisions.[8]

Castro et al. introduced AHI as a predictor of in-hospital mortality in a study involving 462 participants. According to this study, AHI had an AUC of 0.67, a sensitivity of 78%, and a specificity of 42%. A subset of patients with acute decompensated heart failure and decreased ejection fraction was treated with AHI in this study.[7]

By applying AHI to the subset of HFrEF patients who were mechanically ventilated, our study created a more selected population. With an AUC value of 0.82, a sensitivity of 81.4%, and a specificity of 69% for predicting intrahospital mortality, the AHI has a high level of predictive power. In this study, sensitivity and specificity are greater than in the previous one. This is likely due to the use of a more specific population and more stringent inclusion criteria than in the previous study. In this study, researchers excluded patients with malignancies or other diseases with a terminal course. In the preceding study, 18 patients (4%) were diagnosed with cancer. Except for hypertension, the comorbidities obtained in this study showed no statistically significant differences, indicating population homogeneity.

Our study revealed a P value of 0.001 for the effect of hypertension on clinical outcomes. It described an inverse association between hypertension and in-hospital mortality (OR = 0.318, 95% CI = 0.15 - 0.54) This finding is consistent with a Taiwanese prospective study involving 1351 patients in which Meng et al.[9] reported an inverse relationship between pre-existing hypertension and cardiovascular mortality (HR = 0.53; 95% CI = 0.33 – 0.80). According to Ather et al, 10 SBP has a complex, nonlinear relationship with mortality, which is consistent with these findings. This study found that the relationship between TDS and EF was u-shaped in patients with mild-to-moderate EF (30-50%), but linear in patients with severe left ventricular dysfunction (LVEF 30%). These findings may suggest that elevated blood pressure reflects a healthier circulatory system, a strong predictor of survival in systolic heart failure. [11,12]

Increased resting heart rate has long been recognized as a mortality risk factor in patients with heart failure. However, inadequate heart rate response during physiological stress has negative repercussions as well. A limited capacity to increase stroke volume in response to stress is a consequence of heart failure. Separate predictors of clinical outcome are efforts to decrease resting heart rate and increase heart rate in response to stress.[13] This is consistent with the research conducted by Dobre et al.14 From the analysis of the HF-ACTION trial data on 1118 patients with HFrEF (EF 35%) taking beta blockers, it was determined that failure to increase heart rate during exercise trials was represented by a confidence interval (CI) in which every 0.1 decreases in CI 0.6 was associated with a 17% increased risk of all-cause mortality (HR 1.17, 95% CI 1.01–1.36; P=0.036) and a 13% increased risk of cardiovascular death or rehospitalization. In a study conducted by Lancelotti et al15, a high heart rate 24-36 hours after admission in a subset of patients with acute heart failure was associated with a high risk of intrahospital death (subjects who died had a heart rate of 92 22 bpm and those who survived had a heart rate of 78 18 bpm) ; p<0.0001).

Several variables, including the AHI value, P/F ratio, pulse pressure, and heart rate, are believed to be associated with in-hospital mortality based on the results of a multivariate analysis with logistic regression reported in this study. AHI has the strongest predictive ability among these variables (table 8) (AUC = 0.825%, 95% CI = (0.743-0.905%)). Prior research attempted to use blood pressure and heart rate as prognostic factors in acute decompensated heart failure; the relationship between heart rate and prognosis in cardiovascular disease has been well-established for decades. Since the introduction of beta-blockers and ivabradine, heart failure treatment has centered on slowing the heart rate. The interaction between the patient's blood pressure, heart rate, and heart failure medications may have influenced the results. This study nevertheless demonstrated that AHI is more predictive than blood pressure and heart rate alone. The results of a cross-tabulation revealed that patients with admission AHI values of 4.19 had a 9-fold increased risk of mortality (OR = 9.62 (95% CI = 4.23-21.90)).[16]

To determine the effect of heart failure medications on AHI values, a subgroup analysis was conducted. Vasoactive agents (inotropic and vasopressors) are recognized as the cornerstone of cardiovascular disease treatment. In general, these substances have excitatory and inhibitory effects on cardiac and vascular smooth muscle, in addition to metabolic, central nervous system, and autonomic nervous system effects.[17]

It is generally accepted that these vasoactive agents raise blood pressure by increasing CO or SVR. This agent is also known to increase the heart rate so the mode of administration of these drugs can influence AHI values.[18] Table 3 provides information regarding the influence of inotropic administration on AHI values. At the time of admission to the emergency department, 44% of the subjects had received vasoactive agents. Although not statistically significant, the administration of inotropes and vasopressors was associated with an increase in AHI (4.1 ± 1.5 vs. 4.5 ± 1.5, $P = 0.136$). To determine whether inotropes and vasopressors can reduce the predictive value of AHI for in-hospital mortality, however, more research is required. Due to the small sample size, we did not perform a subgroup analysis in this study on patients with a history of beta-blocker use.

Limitation

Limitations exist in this analysis. First, hospital deaths rely on medical records. The data obtained are observational, so we didn't analyze therapy management and intrahospital mortality causality. Because the main purpose of this study was to analyze the usefulness of an index that can be applied as soon as a patient arrives at the emergency department.

The registry does not follow a specific protocol, and blood pressure and heart rate may be measured with different equipment. These results were limited to HFrEF patients.

5. Conclusion

AHI is a practical, objective, and easily accessible predictor of in-hospital mortality in patients with acute decompensated heart failure receiving mechanical ventilation. Prospective research should evaluate these findings in other populations.

In CVCU patients with acute decompensated heart failure, the association between AHI and intrahospital mortality is highly significant. AHI is predictive of intrahospital mortality in patients with acute decompensated heart failure receiving mechanical ventilation in the CVCU at Dr. Saiful Anwar Hospital Malang

6. Declarations

6.1. Ethics Approval and Consent to participate
This study was approved by local Institutional Review Board, and all participants have provided written informed consent prior to involvement in the study.

6.2. Consent for publication
Not applicable.

6.3. Availability of data and materials
Data used in our study were presented in the main text.

6.4. Competing interests
Not applicable.

6.5. Funding source
Not applicable.

6.6. Authors contributions
Idea/concept: DAK, SA. Design: DAK, SA. Control/supervision: SA, AR, BS, VYSP. Literature search: A, AR, BS, VYSP. Data extraction: DAK, SA. Statistical analysis: DAK, SA. Results interpretation: DAK, SA. Critical review/discussion: A, AR, BS, VYSP. Writing the article: DAK, SA. All authors have critically reviewed and approved the final draft and are responsible for the content and similarity index of the manuscript.

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