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Original Article

Scoring system for early detection in pulmonary hypertension type I based on clinical presentation, electrocardiography, and chest X-ray at RSUD dr. Saiful Anwar

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ABSTRACT

Background: In Indonesia, pulmonary hypertension prevalence is 1:10.000 population. Due to its atypical symptoms, often PH patients come as a late presenters thus they have a worse prognosis. The golden standard to diagnose is Right Heart Catheterization (RHC) which is not widely available.
Objectives: To generate a scoring system based on clinical presentation, electrocardiogram, and chest x-ray for early detection.
Methods: A hospital-based cross-sectional survey was conducted in RSUD dr. Saiful Anwar, East Java from July 2020 – November 2023 with data from the medical record in which all variables are obtained at one period. Data were analyzed using bivariate analysis, multiple logistic regression, and Area Under Curve (AUC) from Receiver Operating Characteristic (ROC).
Results: A total of 244 patients who were above 18 years old were conducted RHC at RSUD dr. Saiful Anwar East Java. We found a total score of 12 consisting of Dyspnea on Effort (DOE) score 2, Palpitation score 1, Increasaed P2 score 2, Increased JVP (Jugular vein pressure) score 2, RV (Right Ventricular) Heaves score 2, Right bundle branch block (RBBB) score 1, and Cardiomegaly (CTR >50%) score 2. With a 2 x 2 table, we found that a score of ⩾5 is likely for pulmonary hypertension diagnosis.
Conclusion: Our study is a predictive model with a scoring system that has good sensitivity and specificity in selected populations where one of its limitations is sampling bias thus cannot yet be applied to the general population and needs further research for validation.

1. Introduction

Pulmonary hypertension (PH) is a pathological dysfunction of the pulmonary arteries that can be induced by respiratory and circulatory issues and can occur in a wide range of clinical settings. PH is classified into 5 groups, according to 6th World Symposium on PH. Group 1, the main topic of this research, its prevalence 48-55 cases/million adult, predominantly affecting young adult and female patients.[1,2] Pulmonary hypertension (PH) is defined as an increase in mean pulmonary arterial pressure (mPAP) above normal (> 20 mmHg) and an increase in pulmonary vascular resistance (PVR) above normal in resting conditions.[3,4]

Right heart catheterization (RHC) is the gold standard to identifies pulmonary hypertension as an increase in resting mean pulmonary artery pressure (mPAP) of more than 20 mm Hg. At repose, the mean mPAP is 14.3 mm Hg, with a normal upper limit of approximately 20 mmHg.[3,5] Predictors of worse outcomes including WHO FC III-IV, intolerance of excersie measured by 6-minute walking distance or VO_2 max, laboratory findings (NT-proBNP > 500 pg/mL, C-reactive protein > 10 mg/mL), echocardiography findings of RV failure or dysfunction, and history of hospitalization due to RHF, also in patients with iron deficiency. Thus, it is paramount for healthcare providers to deliver early recognition of the disease for better outcome and prognosis.[2,6–9]

2. Methods

Study design

A cross-sectional study was conducted in RSUD dr. Saiful Anwar of East Java province during June 2020 to November 2023. Data were analyzed using bivariate analysis, multiple logistic regression, and Area Under Curve (AUC) from Receiver Operating Characteristic (ROC).

Participants & eligibility criteria

During the time frame of data collection, 291 data were collected but only 249 data were eligible. All patient who were conducted right heart catheterization (RHC) and is above 18 years old are included and who were diagnosed with PH other than type I or the data were not complete were excluded.

Data collection

A total 291 data of patients who underwent RHC at RSUD dr. Saiful Anwar were collected during June 2020 – November 2023 through secondary data from medical records at one time of inpatient period. Inclusion criteria are patients above 18 years old and who are diagnosed with PH based on RHC, Exclusion criteria were if there is a lack of data or the patient was diagnosed with PH other than type I. 249 patients were eligible.

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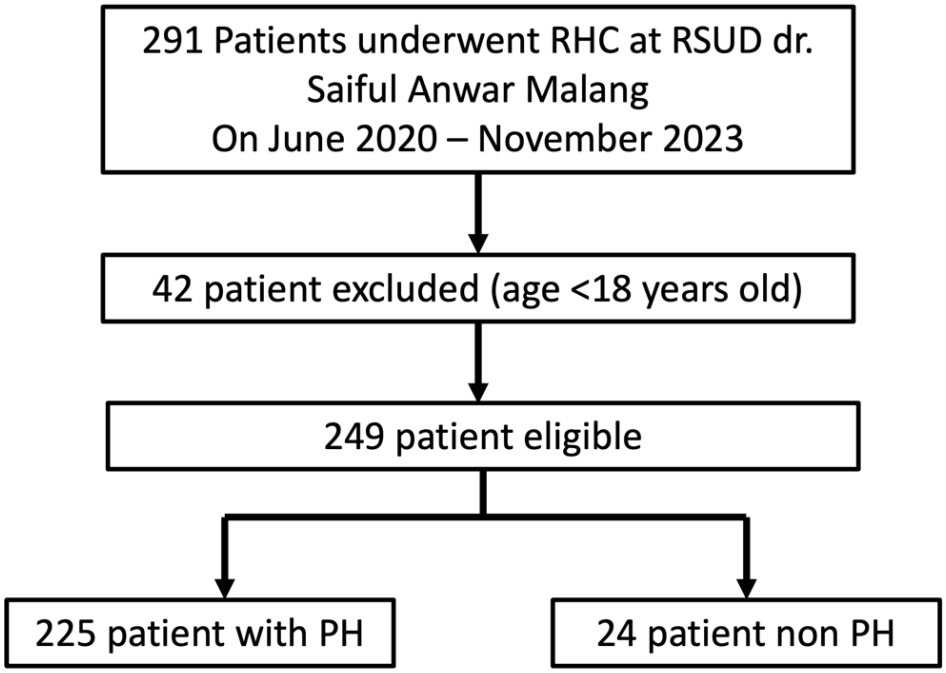

Figure 1. A flowchart of patients selection in our study
PH: Pulmonary Hypertension; RSUD: Rumah Sakit Umum Daerah

Table 1. Data on clinical features, electrocardiography and chest x-rays in this study.

Factors	Pulmonary Hypertension		p
	Yes (n=225)	No (n=24)	
Demographic Data			
Age, median (IQR)	31 (21)	28 (18)	0,086[a]
Male	45 (20,0%)	4 (16,7%)	0,697[b]
Female	180 (80,0%)	20 (83,3%)	0,697[b]
Subjective			
DOE	197 (87,6%)	3 (12,5%)	0,000[b]
Palpitation	81 (36,0%)	3 (12,5%)	0,030[b]
Syncope	16 (7,1%)	0 (0%)	0,998[b]
Ortopneu	15 (6,7%)	0 (0%)	0,999[b]
Chest Pain	4 (1,8%)	0 (0%)	0,999[b]
PND	64 (28,4%)	0 (0%)	0,997[b]
Hemoptysis	9 (4,0%)	0 (0%)	0,999[b]
Abdominal distension	5 (2,2%)	0 (0%)	0,999[b]
Edema	16 (7,1%)	0 (0%)	0,998[b]
Dizzines	7 (3,1%)	0 (0%)	0,999[b]
Fatigue	144 (64,0%)	5 (20,8%)	0,000[b]
Klinis Objektif (pemeriksaan Fisik)			
Increased P2	165 (73,3%)	3 (12,5%)	0,000[b]
Increased JVP	83 (36,9%)	3 (12,5%)	0,026[b]
Heaves	72 (32,0%)	2 (8,3%)	0,029[b]
Murmur/Gallop	21 (9.3%)	0 (0%)	0,998[b]
ECG:			
P Pulmonal	15 (6,7%)	0 (0%)	0,999[b]
RAD	197 (87,6%)	17 (70,8%)	0,031[b]
S presistent	62 (27,6%)	6 (25,0%)	0,790[b]
RBBB	138 (61,3%)	7 (29,2%)	0,004[b]
RVH	158 (70,2%)	7 (29,2%)	0,000[b]
Chest X-Ray			
CTR > 50%	208 (92,4%)	10 (41,7%)	0,000[b]

[a]*Mann Whitney;* [a]*Logistic regression*

Note: IQR, *interquartile range*; DOE, *dyspnea on exertion*; PND, *paroxysmal nocturnal dyspnea*; JVP, *jugular venous pressure*; RAD, *right axis deviation*; RBBB, *right bundle branch block*; RVH, *right ventricular hypertrophy*.

Table 2. Results of multiple logistic regression analysis to determine the pulmonary hypertension diagnosis score.

Predictor Factor	B	S.E.	p	Exp(B)	95% C.I.for EXP(B)		B/SE	(B/SE)/ 0,13	Score
					Lower	Upper			
DOE	5,180	1,661	0,002	177,756	6,85	4613	3,118603	23,98926	24
Palpitation	3,381	2,072	0,103	29,414	0,507	1706	1,631757	12,55198	13
Fatigue	0,161	1,284	0,900	0,851	0,069	10,534	0,125389	0,964534	1
Loud P2	9,835	3,61	0,006	18,670	15,785	22080000	2,724377	20,95674	21
Increasaed JVP	5,201	2,084	0,013	181,49	3,055	10780	2,495681	19,19755	19
Heave	7,569	2,68	0,005	0,001	0	0,099	2,824254	21,72503	22
RAD	1,734	1,532	0,258	5,664	0,281	114,077	1,131854	8,706568	9
RBBB	1,385	1,774	0,435	3,997	0,123	129,44	0,780722	6,00555	6
RVH	0,885	1,752	0,613	2,423	0,078	75,114	0,505137	3,885669	4
CTR > 50%	8,447	3,201	0,008	4662	8,784	2474000	2,638863	20,29895	20

Note: B, *estimated regression coefficient*; SE, *standard error*; Exp(B), eksponen B; DOE, *dyspnea on exertion*; PND, *paroxysmal nocturnal dyspnea*; JVP, *jugular venous pressure*; RAD, *right axis deviation*; RBBB, *right bundle branch block*; RVH, *right ventricular hypertrophy*

Measure

Data measurements were from secondary data of the medical record. The demographic data included age and gender. The conversion of date of birth into actual age was used to measure the age. Subjective data were taken by anamnesis, objective data were taken by physical examination, and ECG criteria were interpreted by the physician in charge and was recorded on the medical record. The Chest X-ray were interpreted by the radiologist and was recorded on the medical record. The diagnosis of Type I PH was retrieved from medical records, and they were confirmed with RHC.

Statistical analysis

Analysis was performed using the Statistical Package for Social Sciences software (SPSS for Windows, version 16, Chicago, USA). The demographic of age, gender, subjective data, objective data, ECG, and Chest-Xray were analized by Bivariate Chi-square method with significant value of $p < 0.05$. To determine scoring system we use Multivariate analysis with significant value of $p < 0.1$ and the cutoff scoring system using ROC by AUC.

3. Results

Patients selection

During June 2020 to November 2023, a total of 249 patients in our study, consisting of 225 patients with Type I PH and 24 patients with non PH. A flowchart describing eligibility pathway in our study is provided in Fig 1.

Baseline characteristics

The majority of the participants were female (80%) with Type I PH (90%). All patients are above 18 years old. The characteristics of patients with Type I PH and non PH that significant had p value of more than 0.05. This data distribution revealed that data were distributed non-homogenously between Type I PH and non-PH patients.

Main findings

The results of the logistic regression test (unadjusted) of this study (Table 1) show that; from clinical picture variables, electocardiography, and chest x-ray; syncope, orthopnea, chest pain, PND, hemoptysis, abdominal distension, edema, dizziness, murmur/gallop, P pulmonale, and S persistent have a p value above 0.05. Therefore, this variable was not included in the multiple logistic regression test. Meanwhile, the variables DOE, palpitations, fatigue, increased P2, increased JVP, heaves, RAD, RBBB, LVH, and cardiomegaly have a value of $p<0.050$. Therefore, these variables were continued with a multiple logistic regression test (adjusted) to determine the score value of each variable. The results of the multiple logistic regression test showed that DOE, increased P2, increased JVP, heave, and cardiomegaly were independent diagnostic factors ($p<0.10$) while palpitations, fatigue, RAD, RBBB, and RVH were dependent diagnostic factors ($p>0$, 10). The results of determining this score are presented in Table 2. The results of this calculation show that DOE has a score of 24, palpitation has a score of 13, fatigue has a score of 1, hardened P2 has a score of 21, JVP has a score of 19, heave has a score of 22, RAD has a score of 9, RBBB has a score of 6, RVH has a score 4, and cardiomegaly has a score of 20. The recapitulation results of these scores are presented in Table 3. This score has a range of 0-139 points.

The next stage in this research is to determine the cut-off score for diagnosing PH. The score value is entered into the registry data for each patient and the cumulative score is calculated. The value of this cumulative score was then tested for normality and an abnormal distribution of data was obtained in the PH group. Therefore, the data was subjected to the Mann Whitney test. The results of this test showed that PH patients had a higher score than non-PH patients (MD: 54.50; 95%CI: 45.00 – 69.00; $p<0.0001$). This data comparison is presented in scatter bar form in Figure 2.

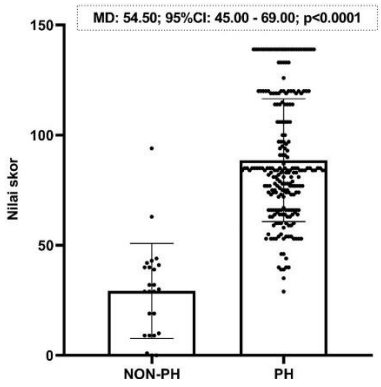

Figure 2. Scatter bar regarding the distribution of pulmonary hypertension diagnosis scores (MD: 54,50; 95%CI: 45,00 – 69,00; p<0,0001). Note, MD, *median difference*; CI, *confidence interval*; PH, *pulmonary hypertension*.

Table 3. Score results for the diagnosis of pulmonary hypertension

Predictor factors	Scoring
DOE	
Yes	24
No	0
Palpitation	
Yes	13
No	0
Fatigue	
Yes	1
No	0
P2 hardens	
Yes	21
No	0
JVP increases	
Yes	19
No	0
Heave	
Yes	22
No	0
RAD	
Yes	9
No	0
RBBB	
Yes	6
No	0
RVH	
Yes	4
No	0
CTR >50%	
Yes	20
No	0

Note: DOE, dyspnea on exertion; PND, paroxysmal nocturnal dyspnea; JVP, jugular venous pressure; RAD, right axis deviation; RBBB, right bundle branch block; RVH, right ventricular hypertrophy

The cut-off score between the PH and non-PH groups in this study was determined using ROC accompanied by calculation of the Youden index. This cut-off value has a sensitivity of 96.44% and a specificity of 91.67%. The cut-off calculation using ROC in this study is presented in Figure 3.

We then implemented this cut-off value of 45 points into the registry data of this study and we found that patients with a score of >45 points had a significant difference compared to patients with a score of ≤ 45 points where patients with a score of >45 points had a higher risk of developing PH was compared with patients with a score of ≤ 45 points (OR: 298.38; 95%CI: 59.62 – 1438.24; p<0.001).

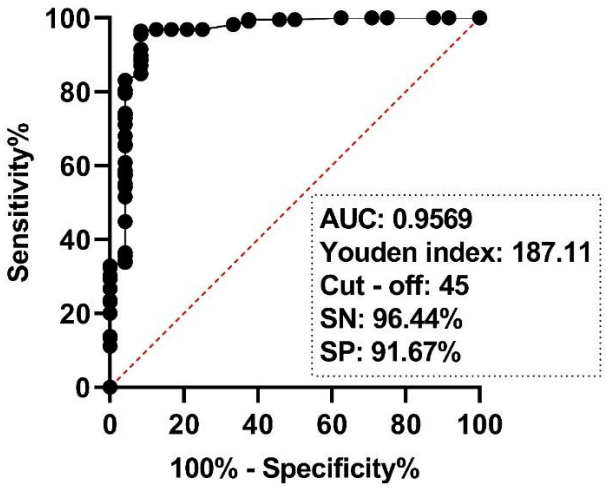

Figure 3. Receiver operating characteristic curve regarding the determination of the cut – off score for the diagnosis of pulmonary hypertension (AUC, 0.9569; Youden index: 187.11; Cut – off score: 45; SN, 96.44%; SP, 91.67%). Note, AUC, area under curve; SN, sensitivity; SP, specificity.

4. Discussion

The characteristics of research patients are described based on proportions, mean with standard deviation in normal data distribution or median with interquartile range in non-normal data distribution. The normality test was used using the Kolmogorov-Smirnov statistical method with α=0.05. If the data has a p value > 0.05, then the data is normally distributed. Then proceed with the data homogeneity/diversity test using the Levene test which aims to show that the data distribution has the same or homogeneous variance. Data is said to be homogeneous if a significance value of α>0.05 is obtained. The next test is logistic regression analysis (unadjusted) to analyze the relationship between the independent variable and the dependent variable Pulmonary Hypertension (PH). The relationship between variables is considered significant if p<0.05 is obtained. Variables that have a p value <0.05 are then subjected to multivariate analysis to determine the scoring system using the multiple logistic regression test method. A p value <0.10 is considered an independent variable while a p value ≥0.10 is considered a dependent variable. Determining the score for each variable is determined by calculating the estimated precision value by dividing the coefficient (B) by the standard error (SE). This value is then divided by the smallest estimated precision number and the results are rounded to the nearest value.

The score value for each patient is then carried out with a t - test with the effect estimate being the mean difference if the data is normally distributed or Mann Whitney with effect estimates being the median difference if the data is not normally distributed. Comparison of score data between groups in this study is presented in scatter bar form. If a significant difference in scores is found between the two research groups, it is followed by calculating the Receiver Operating Characteristic (ROC) accompanied by calculating the area under the curve (AUC) to determine the sensitivity, specificity and Youden index values. AUC value >50% – 60% indicates very weak quality, >60% – 70% indicates weak quality, >70%. – 80% indicates medium quality), >80% – 90% indicates good quality, and >90% indicates very good quality. Next, this data is then calculated for the Youden index where the highest Youden index value is considered the optimal cut-off value for diagnosing PH. This cut-off score data was then converted into categorical data and a chi-squared test was carried out with effect estimates, namely the odds ratio (OR) to determine how big an impact this score had in diagnosing PH. Statistical Package of Social Sciences 17.0 software (SPSS Inc., Chicago, IL, RRID:SCR_002865) and Graphad Prism (GraphPad Software, Boston, MA, RRID:SCR_002798) were used to analyze the data in this study.

5. Conclusion

Based on our observations, this study is the first study to develop scoring as an early detection of PH in Indonesia. This research is a cross-sectional study based on a medical record which is a predictive model attempting to generate a scoring system based on subjective and objective data including symptoms, physical examination, chest x-ray and electrocardiogram. In this study is specifity and sensitivity were reliable in the selected population (Type I PH). Due to its data selection bias and inter-variability observer, validation tests are needed in the general population so that this score can be applied clinically for early detection of PH. A larger data set with a larger comparison population (non PH) is needed.

6. Declaration

6.1 Ethics Approval and Consent to participate
The study protocols were approved by the Institutional Review Board, RSUD dr. Saiful Anwar, East Java, Indonesia (No: 070/36818/102.7/2023). Data collection was from medical record.

6.2. Consent for publication
Not applicable.

6.3 Availibility 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: HM, AF. Design: HM, AF. Control/supervision: HM, AF. Data collection/processing: LUK. Analysis/interpretation: LUK, HM, AF. Literature review: HM, AF. Writing the article: LUK. Critical review: HM, AF. All authors have critically reviewed and approved the final draft and are possible for the content and similarity index of the manuscript.

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