ORIGINAL ARTICLE

DIAGNOSTIC ACCURACY AND PREDICTION OF COVID-19 OUTCOME USING ARTIFICIAL INTELLIGENCE BASED ON RADIOLOGICAL DATA, CLINICAL AND LABORATORY PARAMETER AT DR. SARDJITO GENERAL HOSPITAL, YOGYAKARTA

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ABSTRACT

Introduction: The application of the “color heat-map” method through identifying and analyzing chest X-ray images transferred into AI (artificial intelligence) to generate scores. The aim of this research to was to evaluate the diagnostic accuracy of artificial intelligence scores of Chest X-Ray for predicting the clinical outcome of COVID-19 patients and establishing a scoring system using predictor variables based on AI scoring data based on chest X-rays, clinical parameters, and laboratories of COVID-19 patients.

Methods: A retrospective study collected data from hospitalized COVID-19 patients in Dr. Sardjito General Hospital, Yogyakarta, between 2020 and 2022. The data collected is clinical, laboratory parameters, patient outcomes, and values from AI Chest X-Ray readings. Artificial intelligence was used to detect radiographic abnormalities using CAD4COVID-Xray software (Thirona, Nijmegen, Netherlands). Receiver operator curve (ROC) to evaluate the predictive value of the AI probability score and AI Affected Lung Area score. Multiple logistic regression analysis selected some variables to develop the scoring model.

Results: Four hundred forty-nine (449) patients were included in the study: 237 males (52,8%), median age 56 years (IQR = 45-65). ROC analysis shows that the AI probability score (AUC = 0.875, CI 95% 0.801-0.948) and AI ALA score (AUC = 0.836, CI 95% 0.766-0.906) have sufficient discrimination ability to determine the degree of disease severity of COVID-19 confirmed subjects. Multiple logistic regression analysis from clinical, laboratory, and clinical outcomes showed that this scoring system uses seven variables (5 clinical and two laboratory variables) and has a good prognostic ability to predict the severity of COVID-19 patients. Based on the stratification of scoring results, we found that the scoring value of low-risk patients (1-2 points) had a mortality proportion of 7.8.%, moderate risk ((3-5) points) had a mortality proportion of 38.7%, and high-risk ((6-9) points) had a mortality proportion of 76.9%.

Discussion: Using an AI-based score derived from radiographic, clinical, and laboratory parameters may be beneficial to estimate prognosis in confirmed COVID-19 patients.

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DIAGNOSTIC ACCURACY AND PREDICTION OF COVID-19 OUTCOME USING ARTIFICIAL INTELLIGENCE BASED ON RADIOLOGICAL DATA, CLINICAL AND LABORATORY PARAMETER AT DR. SARDJITO GENERAL HOSPITAL, YOGYAKARTA

INTRODUCTION

COVID-19 caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) is a disease that attacks the respiratory tract with a very high rate of spread.[1] The Gold Standard test to establish the diagnosis of COVID-19 recommended by the World Health Organisation (WHO) is the nucleic acid amplification test (NAAT) with the reverse-transcriptase polymerase chain reaction (RT-PCR) method.[2]

Chest Computerized Tomography (CT) is one of the radiography alternatives for screening Covid-19 patients whereas RT PCR result testing is negative, this might happen because RT PCR sensitivity is lower than Chest CT[3]. However, not all healthcare facilities have access to Chest CT, the other available option is Chest X-Ray. [4] Chest X-Ray examination is more convenient because of simpler equipment and saving time than the RT-PCR examination. Chest X-Ray in patients confirmed with COVID-19 shows bilateral consolidation at the bottom with a peak on days 10–12 after symptom onset and 69% of sensitivity.[5] Chest X-Ray results show a correlation between ground glass opacity (GGO), consolidation, and reticular-nodular opacity as independent predictors for patients confirmed positive for COVID-19. [6]

One of the relevant AI-based software developed during the COVID-19 pandemic was CAD4COVID-Xray, it is developed by Thirona adapting the system of CAD4TB software version 6.[7] The application of the "color heat-map" method through identifying and analyzing chest X-ray images transferred into AI (artificial intelligence) to generate scores. The aim of this research to was to evaluate the diagnostic accuracy of artificial intelligence scores of Chest X-Ray for predicting the clinical outcome of COVID-19 patients and establishing a scoring system using predictor variables based on AI scoring data based on chest X-rays, clinical parameters, and laboratories of COVID-19 patients.

Method

Study Design and Participants

A retrospective study collected data from hospitalized COVID-19 patients in Dr. Sardjito General Hospital, Yogyakarta, between 2020 and 2022. Data collected from the electronic medical records of 449 patients aged ≥ 18 years, hospitalized due to COVID-19 which included discarded and confirmed, have initial Chest X-Ray data, tests of real-time Reverse Transcriptase Polymerase Chain Reaction (RT-PCR). The specimens were collected from a nasopharyngeal swab during admission or in the early phase of hospitalization.

Data Collection

The data collected were clinical including symptoms, vital signs, comorbidities, laboratory parameters, patient outcomes, and values from AI Chest X-Ray readings. Artificial intelligence was used to detect radiographic abnormalities using CAD4COVID-Xray software (Thirona, Nijmegen, Netherlands). The severity of COVID-19 cases was classified based on the Local Indonesia guideline which is in line with the severity stratification COVID-19 guideline from WHO.

Statistical analysis

The demographic quantitative and qualitative data were assessed with median and frequency, respectively. The chi-square test or Fisher's exact test was used to compare variables with the patient outcome. Receiver operator curve (ROC) to evaluate the predictive value of the AI probability score and AI Affected Lung Area score. Multiple logistic regression analysis selected some variables to develop the scoring model. The analysis was done at a significance level of less than 0.05 with a 95% confidence interval and performed using SPSS version 26.0.

Ethics

This study was reviewed and approved by the Medical and health research ethics committee (MHREC) Faculty of Medicine, Public Health and Nursing, Universitas Gadjah

Mada – DR.Sardjito General Hospital Ref No KE/KF/0900/EC2022.

Results

Characteristics

Four hundred forty-nine (449) patients were included in the study (Table 1): 237 males (52,8%), median age 56 years (IQR = 45-65). Most half of the patients had positive results of RT-PCR test 307 (68.4%) and deceased (37.6%) at the end of the treatment. The most common comorbidities are hypertension (26,9%), diabetes (31%), cardiovascular disease (12.2%), and cancer (8.9%). The mean of the AI probability score and AI Affected Lung Area score was 64.54 (0-100) and 35.26 (00-99.9) respectively. The AI successfully read 447 chest X-Ray data and Figure 1 shows the heatmap method to detect radiographic abnormalities with the CAD4 COVID-X Ray software.

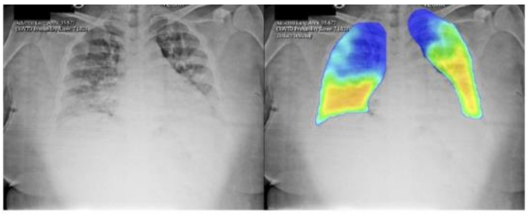


Figure 1. Heatmap method to detect radiographic abnormalities with the CAD4 COVID-X Ray software

Figure 2 and Tabel 2 show the result of ROC analysis that the AI probability score (AUC = 0.940, CI 95% 0.915-0.964) and AI ALA score (AUC = 0.121, CI 95% 0.082-0.159) discrimination ability was not sufficient to determine the severity of COVID-19 confirmed subjects.

Table 1. Demographic And Clinical Characteristics Of COVID-19 Patients

Variable	Total patients (N = 499)	Variable	Total patients (N = 499)
Sociodemographic characteristics		**Laboratory Results**	
Man	237 (52.8)	RT PCR (Positive)	307 (68.4)
Woman	212 (47.2)	Hemoglobin (g/dL)	12 (11.5- 18)
Age (years)	54.68 (18-90)	Leukocytes (10^3 cells/μL)	8.1 (6.9 – 10.30)
BMI (kg/m2)	24.02 (13.30 -70.25)	Neutrophils (10^3 cells/μL)	6.33 (4.27-9.08)
Smoke	8 (1.8)	Lymphocytes (10^3 cells/μL)	1.4 (08.9 – 1.0)
Vaccination Status		NLR	4.7 (3.47 -10.2)
First Dose	50 (11.2)	Thrombocyte (10^3 cells/μL)	245 (190- 303)
Second Dose	45 (10)	SGOT (U/L)	48.62 (28.0 – 74.0)
No Vaccine	353 (78.8)	SGPT (U/L)	35.00 (22.0 -65.0)
Year Infected		Ureum (mg/dL)	16.8 (11.2 -28.8)
2020	8 (1.8)	Creatinine (mg/dL)	0.99 (0.74 -1.41)
2021	336 (74.8)	Sodium (mmol/L)	135 (107.0 -175.0)
2022	105 (23.4)	Potassium (mmol/L)	4.12 (3.74 -4.58)
History of the disease		**Radiological Results**	
Hypertension	121 (26.9)	Pneumonia	
Diabetes Mellitus	139 (31)	Unilateral	8 (1.8)
Coronary Heart Disease	8 (1.8)	Bilateral	334 (74.4)
Cardiovascular Disease	55 (12.2)	Pleural effusion	29 (6.5)
COPD	5 (1.1)	*Probability Score*	64.54 (0-100)
Asthma	6 (1.3)	*Affected Lung Area Score*	35.26 (00-99.9)
Pulmonary Tuberculosis	22 (4.9)	**Complications and Coincidence**	
Chronic Kidney Disease	38 (8.5)	Sepsis	42 (9.2)
Chronic Liver Disease	4 (0.9)	Sepsis shock	22 (4.9)
Cerebrovascular Disease	12 (2.7)	ARDS	20 (4.5)
Autoimmune	8 (1.8)	Secondary Infection	8 (1.8)
HIV/AIDS	8 (1.8)	**Admission conditions**	
Cancer	40 (8.9)	Severity	
Vital Signs		Mild	36 (9.5)
TDS (mmHg)	127 (71 -270)	Moderate	199 (52.4)
TDD (mmHg)	76 (34 -142)	Severe	135 (35.5)
MAP (mmHg)	93 (51-178)	Critically ill	10 (2.6)
Pulse (x/min)	97 (26-170)	**Outcome**	
Breathing Rate (x/min)	24 (16-47)	Length of stay (days)	8 (1.0 – 41.0)
Body Temperature (ºC)	36.6 (33.5 – 75.00)	Mortality	
Oxygen Saturation (%)	92 (80-100)	Survived	280 (62.4)
Clinical symptoms		Deceased	169 (37.6)

Variable	Total patients (N = 499)	Variable	Total patients (N = 499)
Symptom Onset (Day)	4.96 (1-30)		
Fever	276 (61.5)		
Cough	317 (70.6)		
Pharyngitis	51 (11.4)		
Rinorea	58 (12.9)		
Anosmia/Hyposmia	53 (11.8)		
Myalgia	38 (8.5)		
Headache	68 (15.1)		
Malaise	84 (18.7)		
Anorexia	101 (22.5)		
Diarrhea	68 (15.1)		
Nauseous	102 (22/7)		
Vomit	106 (23.6)		
Abdominal pain	51 (11.4)		
Shortness of breath	216 (48.1)		
Chest pain	92 (20.5)		
Loss of Consciousness	26 (5.8)		

Table 2. AUC, SD, CI 95%, and p-values for Positive PCR

	AUC	SD	P-Value	CI 95%
AI Probability Score	0.940	0.012	0.000	0.915-0.964
AI ALA Score	0.121	0.020	0.000	0.082-0.159

Figure 3 and Tabel 3 show the result of ROC analysis that the AI probability score (AUC = 0.875, CI 95% 0.801-0.948) and AI ALA score (AUC = 0.836, CI 95% 0.766-0.906) have sufficient discrimination ability to determine the degree of disease severity of COVID-19 confirmed subjects.

Table 3. AUC, SD, CI 95%, and p-values for Severity

	AUC	SD	P-Value	CI 95%
AI Probability Score	0.836	0.036	0.000	0.766-0.906
AI ALA Score	0.875	0.037	0.000	0.801-0.948

Figure 4 and Tabel 4 show the result of ROC analysis that the AI probability score (AUC = 0.875, CI 95% 0.801-0.948) and AI ALA score (AUC = 0.836, CI 95% 0.766-0.906) discrimination ability not sufficient to determine the mortality of COVID-19 confirmed subjects.

Table 4. AUC, SD, CI 95%, and p-values for Mortality

	AUC	SD	P-Value	CI 95%
AI Probability Score	0.578	0.034	0.025	0.592-0.721
AI ALA Score	0.656	0.033	0.000	0.512-0.644

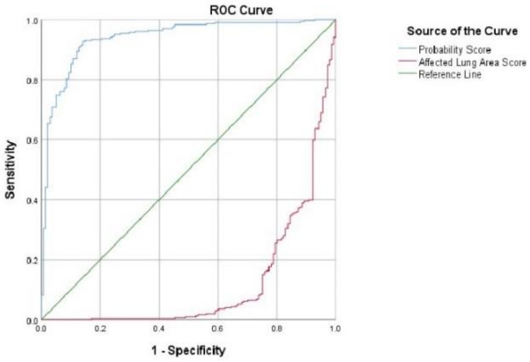


Figure 2. AI scoring ROC Curve for Positive PCR

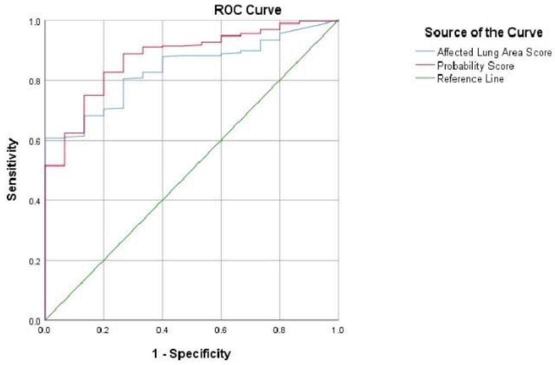


Figure 3 AI scoring ROC Curve for Severity

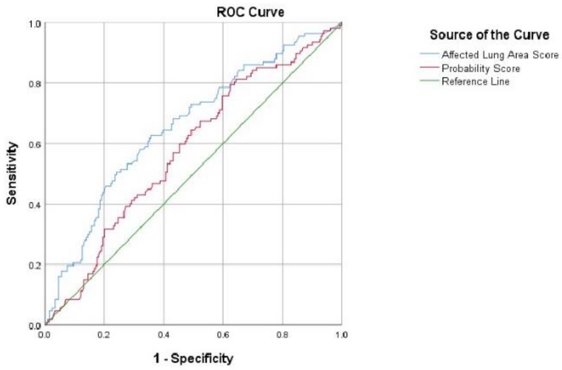


Figure 4 AI scoring ROC Curve for Mortality

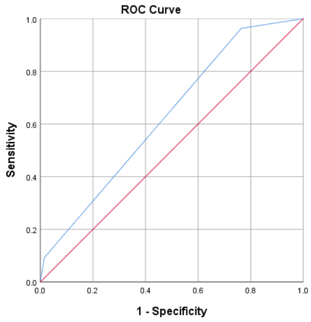


Figure 5 Predictive Scoring ROC Curve for Mortality

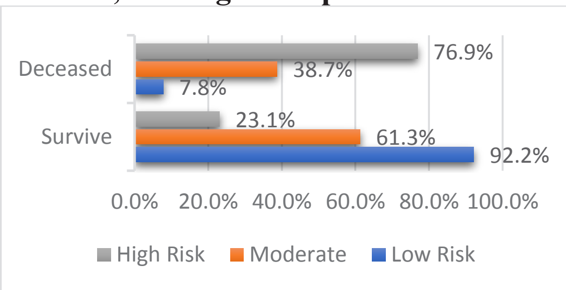
Multiple logistic regression analysis from clinical, laboratory, and clinical outcomes showed that this scoring system has seven variables (five clinical and two laboratory variables) shown in Table 5 and has a good prognostic ability to predict the mortality of COVID-19 patients shown in Figure 5.

Table 5. Predictive Scoring ROC Curve for Mortality

No	Predictor	β	aOR	IK 95%		P -value	Score
				Lower	Upper		
1	Gender	-0,876	0,417	0,196	0,886	0,023	-1
2	Anosmia	1,637	5,138	1,365	19,335	0,015	2
3	Headache	0,943	2,567	0,923	7,141	0,071	1
4	Abdominal Pain	-1,656	0,191	0,049	0,744	0,017	-2
5	Loss of Consciousness	-1,771	0,170	0,034	0,848	0,031	-2
6	Ureum (mg/dL)	0,024	1,024	0,996	1,052	0,092	1
7	Sodium (mmol/L)	-0,123	0,885	0,828	0,945	0,000	-1

Based on the stratification of scoring results, we found that the scoring value of low-risk patients (1-2 points) had a mortality proportion of 7.8.%, moderate risk ((3-5) points) had a mortality proportion of 38.7%, and high-risk ((6-9) points) had a mortality proportion of 76.9% shown in Figure 6.

Figure 5. The proportion mortality in low, medium, and high-risk patients.



Discussion

This retrospective study shows that we put interest in optimizing the Chest X-Ray with Artificial Intelligence because most of the available literature focuses on the potential of CT to help predict the severity of COVID-19 patients. Our study explores the potential variable to develop a scoring system that includes demography, clinical, vital signs, and laboratory. The scoring system that we developed in this study shows that gender as man, symptoms like anosmia headache, abdominal pain, and loss of consciousness were risk factors that can help to predict the probability of severity and mortality of COVID-19 patients. While this finding shows different variables compared with the study in China[8] that age and d-dimmer were the good parameters that could help the clinician to identify COVID-19 patients in the early stage.

This study also evaluated the performance of an AI System to detect abnormalities related to COVID-19. Our study shows that IA was a good tool to predict the probability of severity rather than predicting the probability of morbidity of COVID-19 patients. This finding shows the potential to help the radiologist work efficiently with integrated AI, clinical and laboratory data. The result of the AI Score of Chest X-Ray seamlessly can reduce errors, and help radiologists recognize the sign of COVID-19 from the Chest X-ray heat map imaging. This will contribute to situations where the number of radiologists is limited.[9] Another study shows that deep-learning convolutional neural network (CNN) CNN accurately stages disease severity on portable chest x-ray of COVID-19 lung infection. [10] This will support utilizing AI in clinical settings, and this also will help the physicians/ emergency teams to triage patients, risk assessment, allocate resources, monitor disease progression, and plan treatment.

The strength of our study is we elaborate more variables including clinical outcome, and laboratory, and optimized the benefit of the AI scoring system to read Chest X-rays. Whereas some studies only explore one area which is AI to read the X-Ray, and others studies explore only two areas including clinical and Chest X-Ray to predict the severity and mortality of COVID-19 patients[11]. This approach has great potential to predict the severity and mortality of COVID-19 patients. The main limitation of our study is only involved in one hospital one of the hospitals that is the main referral hospital in the Daerah Istimewa Yogyakarta Province, so the severity is mostly moderate and severe.

Conclusion

Using an AI-based score derived from radiographic, clinical, and laboratory parameters may be beneficial to estimate prognosis in confirmed COVID-19.

Acknowledgment

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