ORIGINAL ARTICLE

D-Dimer and Brixia Score to Mortality in COVID-19 Patients

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ARTICLE INFO

Article history:
Received 4 August 2023
Received in revised form
23 February 2024
Accepted 15 May 2024
Available online 31 May 2024

Keywords:
Brixia score,
COVID-19 mortality,
D-dimer,
Infectious disease.

Cite this as:
Falyani SA, Pratiwi SD, Setyawan UA, *et al*. D-Dimer and Brixia Score to Mortality in COVID-19 Patients. *J Respi* 2024; 10: 99-106.

ABSTRACT

Introduction: Coronavirus disease 2019 (COVID-19) is a highly contagious severe and acute respiratory syndrome caused by the SARS-CoV-2 virus. A variety of factors can increase a patient's risk of death, including coagulopathy characterized by increased D-dimer levels. Brixia scores could be one of the determinants of COVID-19 severity, as assessed by chest radiographs. This study aimed to analyze chest radiographic severity based on the Brixia score at the degree of coagulation based on D-dimer in mortality of COVID-19 patients who were hospitalized.

Methods: This cohort retrospective study was conducted at Dr. Saiful Anwar General Hospital, Malang, using an observational cross-sectional design. The study included 300 medical records of COVID-19 patients who passed away while hospitalized. The data were analyzed using the Wilcoxon test, and the results were also tested for Spearman correlation to determine the relationship between variables.

Results: Significance results of median D-dimer were found by age and severity of COVID-19 (p-values 0.015 and 0.002), and median Brixia scores by age, gender, severity of COVID-19, and length of treatment (p-values 0.001, 0.001, 0.001, and 0.005). The results were also compared with normal values, which were significant (p = 0.000). Spearman correlation test results between the final D-dimer and the initial Brixia score (p = 0.005).

Conclusion: The research results display a retrospective study of the correlation between D-dimer and Brixia score values and outcomes in COVID-19 patients. Higher D-dimer values and Brixia scores on admission were shown to be associated with mortality.

INTRODUCTION

Coronavirus disease 2019 (COVID-19) is a severe and highly contagious acute respiratory condition caused by the coronavirus family member's severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).[1] COVID-19 has a broad clinical spectrum, ranging from asymptomatic to severe cases requiring immediate care. The death rate for COVID-19 patients in urgent settings ranges between 20% and 90%. The most prevalent clinical symptoms of COVID-19 patients in critical condition include acute respiratory distress syndrome (ARDS), acute kidney injury (AKI), cardiomyopathy, thrombotic issues (such as pulmonary embolism), sepsis, and septic shock. Older age, other concomitant illnesses (hypertension, diabetes mellitus, heart disease, and lung disease), a higher sequential organ failure assessment (SOFA) score, and D-dimer levels all increase the risk of disease severity and death from COVID-19.[2]

D-dimer is produced during the coagulation and breakdown of blood. When blood clots break apart, D-dimer is released.[3] A critical degree of COVID-19 patients may show systemic hyperinflammation or a cytokine storm and coagulation disorders. Elevated D-dimer and fibrin breakdown product levels often characterize coagulation abnormalities in COVID-19. Several studies have found a correlation between systemic hyperinflammation and an aberrant coagulation profile, which can lead to life-threatening consequences, such as pulmonary embolism (EP).[3] According to

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Jurnal Respirasi (Journal of Respirology), p-ISSN: 2407-0831; e-ISSN: 2621-8372.
Accredited No. 200/M/KPT/2020; Available at https://e-journal.unair.ac.id/JR. DOI: 10.20473/jr.v10-I.2.2024.99-106

several studies, the prevalence of EP in hospitalized COVID-19 patients ranges from 2.6% to 8.9%.[3] In critical condition of COVID-19 patients, the incidence of EP jumps to 30-60% even though the patients are already on anticoagulants. Postmortem autopsy data on 12 patients in Germany stated that 58% of patients had venous thromboembolism (TEV).[3]

Emerging evidence of hypercoagulability, thrombosis, and coagulopathy in COVID-19 patients has important prognostic consequences. COVID-19 has the most significant impact on the lungs. Microthrombotic pulmonary lesions are twice as common in severe COVID-19 patients as in non-COVID-19 extremely sick patients.[4] Another study found microthrombotic pulmonary lesions in critically ill COVID-19 patients, as well as disseminated intravascular coagulation (DIC) situations in 71% of COVID-19 patients who passed away.[5] As a result, effective anticoagulation therapy is necessary in COVID-19 patients with moderate, severe, or critical disease.

Radiological screening of patients with clinical-epidemiological suspicion of COVID-19 is required to assess thoracic involvement quickly. Most Italian hospitals utilize chest X-ray (CXR) as a first-line approach because it produces fast results, especially when portable X-ray devices are used, which reduce patient movement and the risk of cross-infection.[6] As shown in the CXR, most COVID-19 patients have pneumonia. Brixia scores assess pulmonary parenchymal abnormalities based on the degree of consolidation of lung tissue.

Several studies connect the association between Brixia score and mortality in COVID-19 patients. However, the role of D-dimer and Brixa scores in COVID-19 patients has yet to be thoroughly investigated. This study aimed to analyze chest radiographic severity based on Brixia score at the degree of coagulation based on D-dimer in the mortality of COVID-19 patients hospitalized at Dr. Saiful Anwar General Hospital, Malang.

METHODS

This study used a cohort retrospective observational cross-sectional design. It was a subset of the research analysis of COVID-19 inpatient mortality at Dr. Saiful Anwar General Hospital, Malang. Patients who passed away between January and July 2021 were studied in the isolation room at Dr. Saiful Anwar General Hospital, Malang, using medical record data and hospital information systems.

COVID-19 patients admitted to Dr. Saiful Anwar General Hospital, Malang, were included as the sample population. The study participants were deceased patients with verified instances of COVID-19. Patients with positive nasal and oropharyngeal swab results utilizing reverse transcription polymerase chain reaction (RT-PCR) or SARS-CoV-2 rapid antigen were considered confirmation cases. The degrees of COVID-19 were classified according to the guidelines from the Ministry of Health of the Republic of Indonesia. The length of stay was grouped into <48 hours and >48 hours, and 48 hours was categorized as >48 hours.

The inclusion criteria for this study were patients with positive SARS-CoV-2 PCR results, isolation room inpatients who received therapy from the Department of Pulmonology and Respiratory Medicine, Dr. Saiful Anwar General Hospital, Malang, and patients who passed away during hospitalization. CXR images of lung cancer, interstitial lung disease (ILD), atelectasis, pneumothorax, pleural effusion, and patients under 18 years old were excluded. D-dimer and Brixia scores were examined at the beginning of admission to the emergency room (ER) and the end before passing away as the initial and final values, respectively. Coagulopathy markers were examined using blood samples with standard value limits at Dr. Saiful Anwar General Hospital, Malang, ≤0.5 mg/L for normal values.

The initial D-dimer was checked when the patient first came to the ER, and the final value was the last evaluation when the patient passed away. The standard treatment for coagulants and severity scores based on the Brixia score has yet to be thoroughly investigated. However, the reference limit value for D-dimer in Dr. Saiful Anwar General Hospital, Malang, was used as a standard for administering anticoagulants.

Markers for the severity of COVID-19 were based on quantitative CXR, calculated by dividing the lungs into six fields. The upper zone was the area between the top of the lung and the top of the hilus border. The middle zone was the area between the upper and lower borders of the hilum line, and the lower zone was the area between the hilus's lower border and the lung’s lower border. The assessment used four types of scores, namely 0-3, with value 0 (no infiltrate), 1 (interstitial infiltrate present), 2 (interstitial and alveolar infiltrate present), and 3 (interstitial and alveolar infiltrate present (alveolar is more prominent)).[7] The score was calculated by one experienced thoracic consultant radiologist and one pulmonologist. The initial Brixia scores were checked when the patient first came to the ER, and the final value was the last evaluation when the patient passed away.

Randomized sampling was used in patients who met the inclusion-exclusion criteria in the inpatient department of the COVID-19 isolation unit at Dr. Saiful Anwar General Hospital, Malang. The collected data was processed, evaluated, interpreted, and put into the research sheet. Data was analyzed using statistical tests.

The non-parametric tests were evaluated using Mann-Whitney and Kruskal Wallis with a normal distribution. Spearman's correlation test was performed to evaluate the link between variables. Statistical Package for the Social Sciences (SPSS) version 26 for Windows was used for statistics. This study had passed an ethical review with the letter of ethical review number 400/037/K.3/102.7/2023 from the Ethics Committee of Dr. Saiful Anwar General Hospital, Malang.

RESULTS

The study was conducted at Dr. Saiful Anwar General Hospital, Malang, using medical record data and a hospital information system on patients who passed away between January and July 2021. During the study period, 300 of 546 hospitalized COVID-19 patients were eligible to determine the relationship between coagulation level based on D-dimer and the severity of CXR in the mortality of COVID-19 patients hospitalized at Dr. Saiful Anwar General Hospital, Malang.

Table 1. Sociodemographic Characteristics

Characteristics		n	%
Age	≤40 years old	55	18.3%
	41–59 years old	123	41.0%
	≥60 years old	122	40.7%
Gender	Male	156	52.0%
	Female	144	48.0%
Final Education Level	Uneducated	4	1.3%
	Elementary school	17	5.7%
	Junior high school	38	12.7%
	Senior high school	201	67.0%
	College	40	13.3%
Occupation	Private sector employee	79	26.3%
	Businessman	12	4.0%
	Unemployed	83	27.7%
	Housewife	49	16.3%
	Farm workers	7	2.3%
	State civil apparatus	15	5.0%
	Others	55	18.3%
Smoking History	Smoker	101	33.7%
	Non-smoker	199	66.3%
Domicile	No data	2	0.7%
	Malang (city)	158	52.7%
	Malang (districts)	111	37.0%
	Others	29	9.7%

Based on the data in Table 1 on the characteristics of the degree of severity of COVID-19 and the length of stay of the study subjects, it is known that 1.3% of 300 hospitalized COVID-19 patients had a mild degree of severity, 7.3% had a moderate degree, 58.0% had a severe degree, and 33.3% others had a critical degree. According to the output in the attachment to the analysis results, the degree of severity of COVID-19 patients had altered following treatment at Dr. Saiful Anwar General Hospital, Malang, with as many as 99.7% critical and 0.3% severe. In terms of patient outcomes, all 300 COVID-19 patients were successful. Comparative D-dimer test findings in COVID-19 patients who were hospitalized and passed away based on gender, age, severity of illness, and duration of stay at the hospital can be seen in Table 2.

Table 2. Median D-Dimer Comparison Test Results at the Beginning and End of Hospitalization

Characteristics		n	Initial D-Dimer Median (min-max)	p	n	Final D-Dimer Median (min-max)	p
Age	≤40 years old	41	1.73 (0.45-79.29)	0.015*	24	2.47 (0.95-48.96)	0.000*
	41–59 years old	110	0.96(0.24-35.2)		52	8.68 (0.63-470.6)	
	≥60 years old	100	2.06 (0.38-35.2)		46	2.9 (0.86-35.2)	
Gender	Male	131	1.41 (0.24-79.27)	0.106	63	4.28 (0.63-80)	0.959
	Female	120	1.32 (0.28-35.2)		59	5.12 (0.66-470.6)	
Severity of COVID-19	Mild	4	2.04 (1.33-4.05)	0.002*	3	2.41 (2.35-5.57)	0.734
	Moderate	13	1.61 (0.29-7.42)		11	3.55 (0.86-80)	
	Severe	144	1.19 (0.24-79.27)		78	4.31 (0.63-470.6)	
	Critically ill	90	3.48 (0.45-35.2)		30	7.08 (1.21-35.2)	
Length of Treatment	<48 hours	75	2.55 (0.28-35.2)	0.169	14	4.31 (2.0-47.44)	0.370
	>48 hours	176	1.37 (0.24-79.27)		108	4.38 (0.63-470.6)	

*) With a p-value of 0.05, there was a significant difference

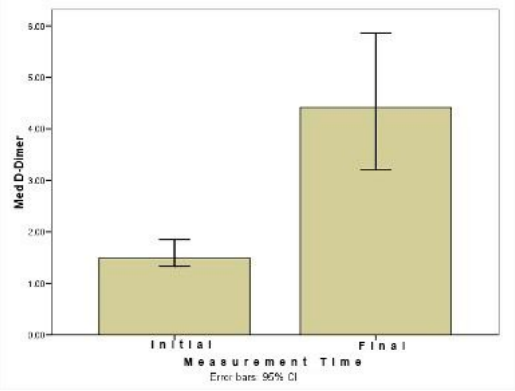

Figure 1. Comparison of Initial and Final D-dimers
The results of the D-dimer comparison are shown via a graph with a line indicating the standard deviation magnitude with p=0.000.

Based on Figure 1, it can be seen that the median of the initial D-dimer was lower than the final D-dimer, with a significant difference between the median of the initial D-dimer and the final D-dimer, using the Wilcoxon test of 0.000 ($p < 0.05$). Thus, it can be concluded that the comparison of the patients' initial D-dimer and the final D-dimer showed a significant difference from the initial D-dimer (median 1.40).

Table 3. Results of Comparison Test of Median Brixia Scores

Characteristics		n	Initial Brixia Score Median (min-max)	p	n	Final Brixia Score Median (min-max)	p
Age	≤40 years old	55	17.0 (12.0-18.0)	0.001*	19	17.0 (11.0-18.0)	0.427
	41–59 years old	123	15.0 (6.0-18.0)		42	16.0 (6.0-18.0)	
	≥60 years old	122	15.0 (7.0-18.0)		44	16.0 (6.0-18.0)	
Gender	Male	156	15.0 (7.0-18.0)	0.001*	51	16.0 (7.0-18.0)	0.886
	Female	144	15.5 (6.0-18.0)		54	16.0 (6.0-18.0)	
Severity of COVID-19	Mild	4	11.0 (7.0-16.0)	0.001*	3	13.0 (8.0-14.0)	0.200
	Moderate	22	12.0 (10.0-13.0)		3	15.0 (13.0-16.0)	
	Severe	174	15.0 (8.0-18.0)		58	16.0 (6.0-18.0)	
	Critically ill	100	16.0 (6.0-18.0)		41	16.0 (6.0-18.0)	
Length of Treatment	<48 hours	101	16.0 (10.0-18.0)	0.005	24	16.0 (6.0-18.0)	0.559
	>48 hours	199	15.0 (6.0-18.0)		81	16.0 (6.0-18.0)	

*) With a p-value of 0.05, there was a significant difference

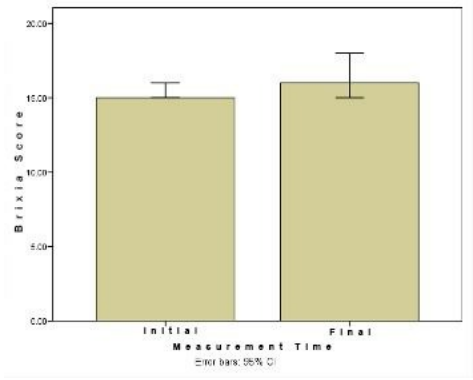

Figure 2. Comparison of Initial and Final Brixia Scores
The results of the Brixia score comparison are shown in a graph with a line showing the standard deviation and a p-value of 0.165 ($p > 0.05$).

According to Figure 2, the median of the initial Brixia score (median 15.0) was somewhat lower than the median of the final Brixia score (median 16.0), with a p-value from the Wilcoxon test results of 0.165 ($p > 0.05$) where the initial Brixia score (median 15.0) was slightly lower than the final Brixia score (median 16.0).

Table 4. Results of the D-Dimer Correlation Test with the Brixia Scores in COVID-19 Patients

Characteristics	Coefficient Correlation	p
Initial D-dimer with initial Brixia score	-0.065	0.303
Final D-dimer with initial Brixia score	0.255	0.005*
Initial D-dimer with final Brixia score	-0.185	0.074
Final D-dimer with final Brixia score	-0.076	0.575

*) With a p-value of 0.05, there was a significant difference

The Spearman correlation test results between the first Brixia score and age revealed a correlation coefficient of -0.211 with a p-value of 0.000 (p = 0.05), indicating a significant association between the initial Brixia score and age. In other words, the higher the first Brixia score, the older the patient, and vice versa, the lower the initial Brixia score, the younger the patient. A correlation coefficient of 0.255 was obtained with a p-value of 0.005 (p = 0.05) for the Spearman correlation test results between the final D-dimer and the initial Brixia score, indicating that there was a significant relationship between the final D-dimer and the initial Brixia score. In other words, the higher the patient's final D-dimer, the higher the patient's initial Brixia score. Conversely, the lower the patient's final D-dimer, the lower the initial Brixia score.

Table 5. Comparison Test Results for D-Dimer Values and Brixia Scores with Normal Values

Characteristics	Mean ± SD	p
Initial D-dimer with normal values	5.386 ± 10.503	0.000*
Final D-dimer with normal values	14.78 ± 3.564	0.000*
Initial Brixia score with normal values	14.46 ± 44.22	0.000*
Final Brixia score with normal values	15.276 ± 3.182	0.000*

*) With a p-value of 0.05, there was a significant difference. The typical D-dimer value at Dr. Saiful Anwar General Hospital, Malang, according to the Department of Clinical Pathology standard value, is 0.05mg/L, and the Brixia score is 0.

The comparative test findings for the D-dimer value and the Brixia score, both with normal values, yielded significant results (p = 0.000). There was a link between the D-dimer value and the Brixia score in COVID-19 patients who passed away during hospitalization.

DISCUSSION

The leading cause of mortality in COVID-19 is acute respiratory distress syndrome (ARDS), which is caused by viral pneumonia. The mechanism of ARDS in SARS-CoV-2 and how host factors contribute to this risk is unknown, but age predicts illness severity and mortality risk.[8]

According to Zhou, *et al*. (2020), patients above 60 years old had more severe symptoms than those below 60 years old.[9] A study shows that the elderly had the highest mortality rate.[10,11] It is assumed to be due to the elderly's proclivity for cytokine storms. These studies are almost equivalent to the findings of this study, which included 81.7% of patients over 40 years old, 40.7% of whom were old.

Several variables strongly increased the severity of the disease discovered in patients with verified COVID-19 clinical profile results at Dr. Saiful Anwar General Hospital, Malang.[12,13] Males were the most affected by COVID-19 and had the most severe symptoms, according to the sociodemographic data. According to this study, 52.0% of the patients were males, while 48.0% were females. Males were higher because females have a more robust innate and adaptive immune system than males. It is similar to the study by Rasmin, *et al*. (2021), which concluded that males had higher plasma levels of innate immune cytokines (such as IL-8 and IL-18) based on differences in viral load, SARS-CoV-2 specific antibody titers, plasma cytokines, and blood cell phenotypes in COVID-19 patients.[14] T-cell activation is much higher in women than in men after SARS-CoV-2 infection. A weak T-cell response may be related to a worse illness prognosis in men.

According to the Centers for Disease Control and Prevention (CDC), working-age people are more vulnerable to exposure since their jobs require them to travel and interact with various people. It is due to close contact and a history of travel to contaminated locations, both risk factors for COVID-19 infection. However, in this study, there was no significant association between working patient groups and the risk of COVID-19 exposure, and the patient's occupation was undoubtedly associated with their educational status.[15]

In terms of smoking history, it is known that 33.7% of 300 hospitalized COVID-19 hospitalized are active smokers, while 66.3% are non-smokers. According to Hoffmann, *et al*. (2020), smoking was associated with the severity and death of COVID-19 patients.[1]

D-dimer levels are associated with mortality in COVID-19 patients. The findings of this study revealed that the mean value of the initial D-dimer was significant by age group and COVID-19 severity, 0.015 and 0.002, respectively. In contrast, the average of the end D-dimer value was significant by age with a p =

0.000. This result is consistent with other studies that showed the D-dimer value was associated with COVID-19 mortality.[16–18]

A coagulopathy is a prevalent pathological disease in COVID-19, characterized by elevated D-dimer levels. Severe COVID-19 instances are related to a greatly increased risk of deep vein thrombosis (DVT) and acute pulmonary embolism. COVID-19 coagulopathy is characterized by pulmonary intravascular coagulation (PIC). PIC develops locally in the lungs, unlike sepsis-induced coagulopathy (SIC) and DIC, which appear as systemic coagulopathy. In the context of COVID-19, disease progression from PIC to SIC or DIC may suggest that the patient's coagulation malfunction has advanced from a local to a systemic direction. However, whether coagulopathy proceeds linearly from PIC to SIC and inevitably to DIC is unknown.[1,2] The PIC concept is identified as macrophage activation syndrome (MAS) related to diffuse immunothrombosis in COVID-19 patients' lung tissue.[19,20]

Elevated circulating D-dimer concentrations indicate pulmonary vascular thrombosis with fibrinolysis, whereas elevated myocardial enzyme concentrations indicate acute ventricular stress induced by pulmonary hypertension. Several studies have found a high infiltration of macrophages and other immune cells in the lung tissue of COVID-19 patients. Thrombosis is typically caused by an imbalance in Virchow's triad, which includes blood vessels, blood flow, and hypercoagulability. By producing a procoagulant state, viral infection can alter the coagulation cascade. Procoagulant factors are released when lung parenchymal and pulmonary vascular endothelial cells become inflamed. This situation will activate the coagulation cascade, resulting in thrombosis and fibrin deposition in the pulmonary arteries. Endothelial cells can be harmed by uncontrolled inflammation.[21] Lack of oxygen also contributes to the thrombosis mechanism in COVID-19 patients. Vasoconstriction and inflammation will occur from this disease. Hypoxemic conditions will activate the hypoxia-inducible factor, which activates cytokines, TF, and plasminogen activator inhibitor-1 (PAI-1), which can cause thrombosis.[22]

The stimulating effect of the blood coagulation mechanism, triggered by endotoxins of gram-negative organisms that cause pneumonia, can raise plasma D-dimer levels. This study discovered that plasma D-dimer levels in pneumonia outpatients, inpatients, and intensive care units (ICU) were strongly connected with pneumonia severity. COVID-19 infection causes a robust inflammatory response, and lung tissue damage is caused by uncontrolled activation of lymphocytes and neutrophils. In the damaged lung, the virulence or persistent presence of COVID-19 causes a microthrombotic pulmonary inflammatory response, endothelial damage, and vascular leakage. Due to the fibrinolytic capacity, a strong fibrinolytic thrombus is formed. Degraded fibrin fragments (D-dimer) enter the blood and are detected in blood samples.[23] High values of more than 2 µg/ml increase the risk of patient death.[24]

The Brixia score can be a predictor of the severity of COVID-19.[25] In this study, 100% of CXR findings in COVID-19 patients who passed away were confirmed to have evidence of pneumonia. Significant results were obtained on the initial hospitalization Brixia score based on age, gender, severity of COVID-19, and length of stay, with successive values of 0.001, 0.001, 0.001, and 0.005. It indicates that the patient's arrival at the hospital was in a severe condition radiologically compared to the normal value of the Brixia score, which was 0. CXR abnormalities are dominated by soil turbidity mixed with lesions that consolidate or form a ground glass opacity (GGO). GGO is a slightly increased opacification of the lung tissue, and the pulmonary vessels are still visible.[26] Consolidation is a pathological process generated from fluid in the alveoli, mucus, blood, cells, or other substances, resulting in lobar, diffuse, or multifocal opacity. Because type II alveolar epithelial cells exhibit large levels of ACE-2, which is a functional receptor for SARS-2, SARS-CoV-2 targets the lungs. SARS-CoV-2 continues its life cycle after binding to type II alveolar epithelial cells and enters host cells via endocytosis or membrane fusion. It replicates in the host cell's nucleus and develops and releases additional virus particles into the cytoplasm. Inflammation of the alveolar walls is caused by viruses that replicate in alveolar epithelial cells. The walls of the alveoli are thickened, suggesting increased opacity in the lungs. The generalized inflammatory process causes fluid secretion to fill the alveoli in both lung fields, increasing lung opacity, and the pulmonary vessels are no longer visible, causing CXR to show a consolidated appearance.[27]

Infected patients with mild symptoms will generally recover after 2-3 weeks. Those who are infected and develop worse, accompanied by ARDS, cause 10-15% to deteriorate in a short time and die due to organ failure. ARDS is a severe respiratory disorder caused by fluid accumulation in the lungs' alveoli, the main symptom of which is severe shortness of breath. SARS-CoV-2 is a coronavirus belonging to the β genus, causing the COVID-19 disease outbreak. SARS-CoV-2 infection can stimulate the host's immune system, resulting in a drop in lymphocytes and an unusual rise in cytokines in patients. SARS-CoV-2 ribonucleic acid

(RNA) and protein interact with various receptors, activating the antiviral immune response and regulating viral replication and dissemination inside the host. On the other hand, an overactive and excessive immune response will result in immunological damage and consequent tissue inflammation.[28]

Maroldi, *et al*. (2020) examined the Brixia score in 953 pneumonia patients with COVID-19 in Italy, in which 524 patients had one CXR, and 429 patients had more than one CXR.[28] The results showed that the Brixia score of patients who passed away was significantly higher than that of patients who recovered. If the Brixia score is more than 9 and does not fall below a value of 7, it is necessary to consider intensive treatment, such as using a ventilator and care in the ICU. In addition, the Brixia score also contributes to predicting patient prognosis if an increase of 3 or more values is obtained.[29]

CXR is the modality of first choice for evaluating COVID-19 pneumonia compared to chest computed tomography (CT) scans because of its availability, ease of implementation, and relatively faster results. The CXR photo scoring system is not recommended for diagnosing COVID-19, especially at the onset of the disease. However, the chest photo scoring system for COVID-19 pneumonia, using either the Brixia score, the simplified radiographic assessment of lung edema (RALE) score, or the lung zone severity score, has a role in evaluating the severity of pneumonia, which can then be used as a basis for management and determining the prognosis of patients with COVID-19 pneumonia.[26]

The results showed a significant difference between the initial and final D-dimer scores, with $p = 0.005$. This result is in line with several previous studies which reported that most patients with COVID-19 experienced increased D-dimer levels due to an excessive inflammatory reaction in lung parenchyma cells and pulmonary vascular endothelial cells. It causes dysregulation in the coagulation system. This condition can lead to thrombosis and degradation of pulmonary vascular fibrin and cause a hypoxemic state that activates hypoxic triggering factors that activate more pro-inflammatory cytokines, tissue factor, and PAI-1, and cause excessive thrombosis indicated by the presence of increased D-dimer.[7]

This study has several areas for improvement. Sampling of D-dimer and Brixia scores in this study was taken at any time, regardless of previous medical history or history of previous therapy. Comorbidities were not analyzed in depth in this study. Therefore, death in patients cannot be ascertained solely due to COVID-19. The use of anticoagulants should have been reviewed in depth in this study. Almost all patients at Dr. Saiful Anwar General Hospital, Malang, received anticoagulant therapy according to the severity of COVID-19 but did not specify whether to use a particular type of anticoagulant. The final D-dimer value and final Brixia score were not necessarily in the state of the patient who was near death, and it could be 2 days later. Laboratory and radiological evaluations were performed every 3 days per the Medical Practice Guidelines at Dr. Saiful Anwar General Hospital, Malang. However, this study did not specify the day of death and how many days after the evaluation.

CONCLUSION

The study examined the correlation between D-dimer levels and Brixia scores in COVID-19 patients, revealing a significant association between higher D-dimer and Brixia scores and mortality. This suggests that monitoring these parameters could be crucial in predicting patient outcomes and informing treatment strategies. To enhance the management of future COVID-19 pandemics, future research could focus on developing more accurate and early diagnostic tools, such as biomarkers or imaging techniques, to identify those at risk of severe illness. Additionally, studies could explore the efficacy of targeted treatments, such as anticoagulant therapies in optimal doses, in reducing mortality rates among patients with high D-dimer and Brixia scores.

Acknowledgments
The authors would like to thank Dr. Saiful Anwar General Hospital, Malang, and the Department of Pulmonology and Respiratory Medicine, Universitas Brawijaya, for supporting this article.

Conflict of Interest
The authors declared there is no conflict of interest.

Funding
This study did not receive any funding.

Authors' Contributions
Data sampling, analysis, and discussion: SAF, SDP, UAS, DRA, SD, ASL. All authors contributed and approved the final version of the manuscript.

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