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THE CONCORDANCE OF BRIXIA AND RALE SCORES IN EVALUATION OF COVID-19 PNEUMONIA PATIENT USING RADIOGRAPHY IN INDONESIA REFERRAL HOSPITAL

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Abstract

The COVID-19 pandemic has put intense pressure on the healthcare systems. As the lung complication of COVID-19, pneumonia can be assessed by chest radiography which can be used to predict the severity of patient deterioration using Brixia and RALE scores. This research aims to assess the Radiologists' agreement on diagnosing pneumonia COVID-19 by RT-PCR in CXR using the Brixia and RALE score at Dr. Sardjito Central General Hospital from May 2020-January 2021. Two separate radiologists scored initial chest radiographs for RALE and Brixia independently. The analysis assessed included a descriptive analysis of demographic data, and Bland-Altman plots were used to visualize intra-observer agreement. A total of 332 samples were 162 men (48.8%) and 170 women (51.2%), with a mean age of 42.37. The ICC of Brixia score (0.855, CI:0.794-0.895) and RALE score (0.756, CI:0.662-0.812). Bland–Altman analysis revealed a bias of 5.08 ± 6.04 (95% limits of agreement of -6.760 and 16.929) for Brixia and RALE scores and significantly correlated (r=0.886 (p<0.05)). The average score of Brixia (6.29±4.430) and RALE (11.56±9.997) in men was higher than in women. The agreement of Radiologists in diagnosing pneumonia COVID-19 using Brixia and RALE scores with the Bland Altman curve was significant or reliable.

Keywords: *Brixia score; Chest radiography; COVID-19; RALE score*

1. Introduction

First known to appear in Wuhan, China, in December 2019, COVID-19 pneumonia began to spread all over the globe and became a pandemic (Yang et al, 2020). In estimation, more than five million people have been infected worldwide since May 2020 (Yang et al, 2020). Meanwhile, in Indonesia, up to June 2022, more than six million cases have been confirmed, and more than 156,000 deaths have been reported (World Health Organization [WHO], 2022). As the mortality rate of this disease was high, physicians, including radiologists, should be aware of its potential severity, especially in the radiological aspect of COVID-19 pneumonia, to make an accurate diagnosis (Borghesi et al, 2020). At present, polymerase chain reaction (PCR) remains the gold standard. However, the lack of kit availability and the long-awaited result of PCR made early diagnosis of the disease quite difficult (Abo-Hedibah et al, 2021). Some studies assessed the severity of lung pneumonia progression on x-ray examination, as a substitution for chest CT, due to its wide availability and ease (Abo-Hedibah et al, 2021). One of them was designed by Borghesi *et al.* that assessed 100 hospitalized patients until their outcome, named as Brixia-score, could identify the risk

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of developing severe lung disease (Borghesi et al, 2020). Some other studies reported the use of radiographic assessment of lung edema (RALE) score to assess disease outcome and acute respiratory disease syndrome (Zimatore et al, 2021; Kerpel et al, 2020). Even though there was a weakness of chest x-ray (CXR) as stated by the Fleischner Society consensus, it remained the most common modality used in an emergency setting in any patient presenting with respiratory symptoms, including COVID-19 (Kerpel et al, 2020). So, the radiologist's suggestion regarding the severity of pneumonia based on the CXR result was still crucial (Kerpel et al, 2020). The study aimed to assess the reliability of CXRs in patients suspected of COVID-19 at initial presentation in the emergency department (ED) between two radiologists using Brixia and RALE scores.

2. Method

Data collection

This study was done through a retrospective search of the digital hospital archives between May 2020 and January 2021 at Dr. Sardjito Central General Hospital, Indonesia. All CXR of COVID-19 reports and PCR results were retrieved, obtaining a total number of 332 patients. No personal identifiers were included in data collection, and records were anonymized to the statistician. For this retrospective study, ethical approval was obtained from the institutional review board of Dr. Sardjito Central General Hospital and the Faculty of Medicine, Public Health, and Nursing Universitas Gadjah Mada.

Patients Selection

Sample recruitment was carried out consecutively, and all suspected COVID-19 patients admitted to the hospital and undergoing a CXR examination were enrolled in this study. Meanwhile, patients who were proven to have other lung diseases diagnosed with a prior diagnosis (e.g., lung cancer, pulmonary metastases, pulmonary embolism, etc.) were excluded from the study.

Radiograph scoring

The CXRs were analyzed by two experienced radiologists separately. Brixia's scoring system divided the lungs into six regions, and each region's score was summed with a range from 0 to 18. Six regions were divided into two lines, and the first line was drawn at the level of the aortic arch wall and the second line at the level of the right inferior pulmonary vein (Figure 1B). Each region was rated from 0-to three based on the severity of the lesion. Score 0 indicated no lung abnormalities, 2 for interstitial and alveolar infiltrates (interstitial predominance), and 3 for interstitial and alveolar (alveolar predominance) (Yang et al, 2020; World Health Organization [WHO], 2022).

The RALE scoring system divided the lungs into quadrants, vertically by the vertebral column and horizontally by the first branch of the left main bronchus (Figure 1A). Each quadrant was assigned a consolidation score from 0–4 to quantify the extent of alveolar opacities, score 0 for no pulmonary involvement, 1 for lung involvement less than 25%, 2 for lung involvement of 25%-50%, 3 for lung involvement of 50%-75%, and 4 for lung involvement more than 75%. Lung density is scored from 1 to 3 to quantify the overall density of alveolar opacities, scoring 1 (hazy), 2 (moderate), and 3 (dense). The scores for each lung were summed to produce the final RALE score out of 48 (Warren et al., 2018). A total score of 0 was considered negative, while any score from 1-18 (for Brixia) and 1-48 (for RALE) was considered positive.

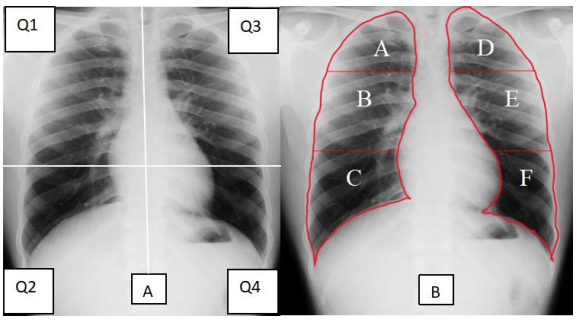

Figure 1. *Lung field division on posteroanterior chest x-ray projection, (A) RALE lung field division onRALE scoring system includings Q1, Q2, Q3, and Q4; (B) Illustration of lung field division on BRIXIA scoring systemincluding lower zone, middle zone, and upper zone(Agrawal et al, 2019)*

Statistical analysis

All analyses were performed on Stata version 15.1 software (Stata Corp., College Station, TX). A *p-value* less than 0.05 is considered statistical significance. Inter-observer reliability was done using the intraclass correlation coefficient (ICC) for RALE and Brixia scores. Brixia and RALE score was presented as

mean and standard deviation in gender and sex group to determine the highest score among groups. The Bland-Altman plots were used to visualize the agreement between the two methods which indicated as a correlation coefficient and p-value.

3. Result and Discussion

The retrospective study using electronic medical records and a PACS system collected 332 chest radiographs from COVID-19 patients between May 2020 and January 2021. The agreement between two radiologists for Brixia and RALE score was good for all two scores, resulting in ICC (Intraclass Correlation Coefficient) of 0.855 (95% CI: 0.794 – 0.895) for Brixia score and 0.756 (95% CI: 0.662 – 0.812) for RALE score, p-value < 0.05.

Table 1. Baseline Characteristics of 332 Chest X-rays

Variables		Brixia Score	RALE Score
	n(%)	mean ± SD*	mean ± SD*
Sex	332(100)		
Men	162(48.80)	6.29 ± 4.43	11.56 ± 9.99
Women	170(51.20)	5.84 ± 4.15	10.47 ± 9.03
Age	332(100)		
< 20	10(3)	5.10 ± 5.32	9.60 ± 8.47
20-60	273(82.20)	5.79 ± 4.12	10.74 ± 9.08
>60	49(14.80)	6.08 ± 4.24	13.69 ± 11.58

**standard deviation (SD)*

A total of 332 chest radiographs, including 162 males (48.8%) and 170 women (51.2%) with a mean age of 42.37 (2-88) years. Most diagnosed patients lay within the age group of 20–60-year-old, about 81 (24.4%), while the least age group was <20 years, about 10 (3.0%) (Table 1).

The majority of the population in this study were women (51.2%) with an average Brixia and RALE score of 5.84±4.152 and 10.47±9.032, respectively (Table 1). The Brixia score had 6 (0-18), while RALE score had 8 (0-45) for median (min-max) values. The Brixia and RALE score was higher in men than in women (6.29±4.430 and 11.56±9.997 vs. 5.84±4.152 and 10.47±9.032). Besides, the higher Brixia and RALE scores were found in the older age group, where both scores were significantly high in the age group > 60-year-old (Table 1). An example of chest x-ray (CXR) report is shown in (Figure 2), in which total Brixia score was of 14 and total score was of 22 for RALE scoring system. The opacity in the lung is illustrate as well in (Figure 2).

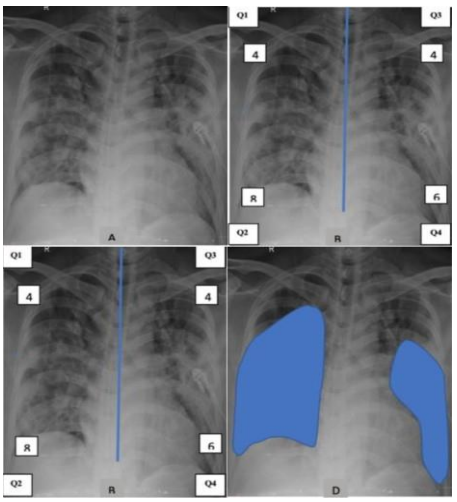

Figure 2. *(A) CXR of 38 years old man with positive COVID-19 by RT-PCR, the opacity was seen at almost the whole lung field, (B) RALE score was 22, (C) The Brixia score was 14. (D) Opacity regions(blue areas).*

The Agreement Between Brixia and RALE Score

From 332 samples, the agreement between two measurements (Brixia and RALE score) on measuring the severity of COVID-19 pneumonia was visualized using the Bland Altman plot (Figure. 3).

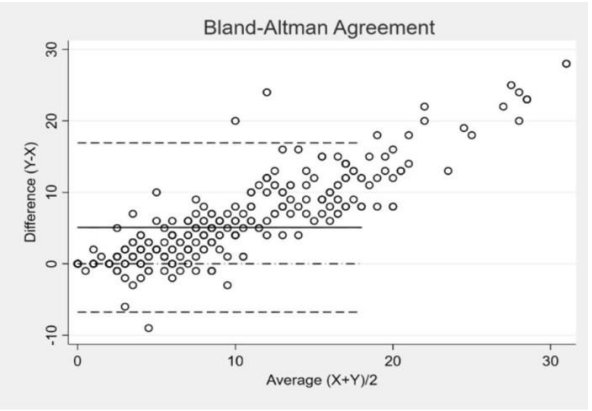

Figure 3. *Bland Altman curve for Brixia and RALE score*

The difference and average of the two measurements were plotted in the Bland Altman analysis. Bland–Altman analysis revealed a bias of 5.08±6.04 (95% limits of agreement of -

6.760 and 16.929) for Brixia and RALE scores (Table 2). The two measurements were significantly correlated with a correlation coefficient of 0.886 ($p<0.05$). Concluded that the severity of COVID-19 pneumonia based on Brixia and RALE score in CXR was significant.

Table 2. The Comparison of Brixia and RALE Score

Variables	Total n	Mean	SD	95% CI†
Brixia	332	6.05	4.28	5.59 – 6.52
RALE	332	11.14	9.50	10.1 – 12.1
Difference	332	5.08	6.04	4.43 – 5.73

**standard deviation (SD), †confidence interval (CI)*

Diagnosis and management of COVID-19 have become challenges in daily practice. In evaluating the patient's severity level, doctors may use several assessment methods, such as laboratory parameters, clinical conditions, and radiological features. One of the radiological assessment methods widely used to determine the severity of COVID-19 infection from chest X-Ray is the Brixia score and RALE score. The assessment of the Brixia score is one of the established methods used to determine the severity of COVID-19 and therefore enables doctors to make quick decisions in determining the patient's status (ICU or Non-ICU) (Signoroni et al, 2021). Brixia score evaluates X-ray of the lungs; providing an assessment in score makes it easier for doctors to provide therapy according to the severity level (Signoroni et al, 2021). The RALE score system was initially used by Warren to assess the extent and severity of pulmonary edema and ARDS. It was then simplified to mRALES by Wong HYF et al (Wong et al, 2020).

Concerning gender, the highest number of subjects from this study were women, 170 (51.2%) patients with a mean Brixia score of 5.84±4.152 and 10.47±9.032 for the RALE score. In the men group, the highest Brixia score was 6.29±4.430 and 11.56±9.997 for RALE, slightly higher than the women group. The previous study found that the men group tends to have more severe cases than women. It has been found that ACE2 levels in men are higher than in women with diabetes or cardiovascular disease (Patel et al, 2013). High expression of organ specific ACE2 receptor protein correlates with organ failure in the study of SARS patients (Yang et al, 2010). Sex hormones and high expression of ACE2 as a coronavirus receptor mediated the resistance effect in women, which is triggered by lifestyle factors such as smoking and alcohol consumption among men (Bwire, 2020).

Gender differences in the adaptive immune system show that women have higher CD4+ T cell counts, stronger CD8+ T cell cytotoxic activity, and increased immunoglobulin B cell production compared to men (Abdullah et al, 2012). These findings imply that women have an increased capacity to enhance humoral immune responses compared to men (Peckham et al, 2020). Women also produce more interferon type 1 (IFN), a potent antiviral cytokine, upon sensing viral RNA as receptor 7 than men, which is essential for the initial reaction in COVID-19 (Mohanty et al, 2022).

Our study found that elderly patients tend to have higher Brixia and RALE scores than younger groups. In the previous study, the mortality percentage of elderly patients (≥ 65 years) was higher than survivors (83.8% vs. 13.2%) (Jin et al, 2020). Increasing age in COVID-19 patients is characterized by higher rates of symptoms of severity at initial presentation. Besides, elderly patients are prone to delay medical care when COVID-19 symptoms arise (Kaleemi et al, 2021).

A current retrospective study in a single institution aimed to assess agreement between 2 radiologists in evaluating the Brixia score and RALE score for assessing the severity level of COVID-19 infection using Bland Altman analysis and ICC (Intraclass Correlation Coefficient). We demonstrated a relatively high inter-rater method of the Brixia score with the ICC method of 0.855 with a CI (0.794 – 0.895), while the RALE score of 0.756 with a CI (0.662-0.812), with p-value 0.00. Bland Altman analysis revealed the mean value of the difference between the Brixia and RALE scores and the 95% confidence interval, with the standard deviation of the average difference between Brixia and RALE scores being 6.04, limit of agreement obtained a lower limit value of -16.929 and the upper limit value of 6.760, with r 0.886 (p 0.00). The present study ascertained that Brixia and RALE scores are reliable and rapid methods to analyze the severity level of COVID-19 infection comparable to other studies (Mancilla et al, 2021; Au-Yong et al, 2022).

We only included all COVID-19 patients confirmed by RT-PCR in the present study. We did analyze all suspected COVID- 19 patients; therefore, we could not analyze the

sensitivity, specificity, and validity of the Brixia and RALE scores. However, a study performed by Nitin Sinha, et al. concluded that both RALES and Brixia scores were not significantly different between COVID-19 positive and COVID-19 negative patients, which reaffirms that CXR Brixia and RALE scores showed no correlation with RT PCR results. This means that Brixia and RALE score scores cannot be used to demarcate suspected COVID-19 patients who are likely to come RT-PCR positive from those who are likely to come negative (Setyawati et al, 2021).

Bhorgesi A and Maroldi R indicated in their published article that Brixia scores were exclusively devised for COVID-19-positive patients and correlated with patient outcomes, as higher Brixia scores were found more in patients who died of COVID -19 rather than those discharged from the hospital ($p \leq 0.002$). A study conducted by Maroldi R et al., also affirmed that the Brixia score correlated with patient outcomes in COVID-19-positive patients and possessed a prognostic value. However, our study did not analyze the correlation between the Brixia score and the RALE score with a clinical condition since we only assessed the improvement or worsening of radiological features from CXR, hence limiting the study. The present study is also limited by a relatively small number of radiologists assessing the CXR. However, our result showed good interobserver agreement and did not differ from those presented in other studies on patients with COVID-19, signifying that those factors did not affect the obtained results (Sinha et al, 2022). The major strength of this study was the larger number of patients included in this study. We believe Brixia and RALE scores are reliable methods to analyze the severity of COVID-19 infection.

4. Conclusion and Suggestion

In conclusion, chest radiographic assessment of COVID-19 patients with pneumonia using the Brixia and RALE score was widely used to determine any risk of developing severe lung disease. It was concluded that the measurement of the severity of the chest x-ray of pneumonia patients with COVID-19 using the Brixia and RALE scores had a good fit with a good correlation coefficient of 0.886 ($p<0.05$). Both scoring systems provide alternative measurements for routine practice. The scoring system was practical to use in a clinical setting to determine patients' status and management at Dr. Sardjito Central General Hospital.

A further prospective study with clinical patient data on follow-up, disease progression, and outcomes such as recovery status, severity, or death is recommended to strengthen the present study's findings.

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