The mortality predicting ability of chest X-ray severity scoring systems in COVID-19 pneumonia

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(Index words: COVID-19 pneumonia, severity, chest X-ray, severity score, mortality prediction)

Abstract

Introduction: Although several chest X-ray (CXR) severity scoring systems are in use to assess COVID-19 pneumonia (CP), inhomogeneity has been observed among the assessment methodologies.

Objectives: To describe and validate severity scoring system based on different features to identify the most suitable scoring system to predict CP severity and outcome.

Method: This retrospective study examined CXRs (n=147) of CP patients (n=85) to calculate severity scores using three scoring systems based on area infiltrated and the density patterns: A, A&D, and New. The best scoring system to predict the mortality was identified using the area under the curve (AUC) and linear regression analysis.

Results: Regardless of the scoring system used, CXR severity has shown a good correlation to clinical CP severity (A: χ^2=6.745; p=0.034; A&D: χ^2=12.404; p=0.002; New: χ^2=10.219; p =0.006). The mortality predictability of all scoring systems were satisfactory with high AUC ("A": AUC=0.685, sensitivity:67.4%, specificity: 54.5% at a cut-off point of 5/8; positive predictive value (PPV): 40.3%, negative predictive value (NPV): 78.6%"; A&D": AUC=0.748, sensitivity: 69.6%, specificity: 61.4% at a cut-off point of 7/16, PPV: 45.1%, NPV: 81.6%; "New": AUC=0.727; p≤0.001, sensitivity:67.4%, specificity:68.3% at a cut-off point of 18/48, PPV: 49.2%, NPV: 82.1%). Additionally, the mortality predicting ability of the "New" scoring system was higher than the other two systems.

Conclusion: COVID-19 pneumonia severity assessed with the CXR severity scoring systems correlated significantly with clinical severity and outcome. Overall, the "New" CXR severity scoring system is comparatively better at predicting the mortality of COVID-19 pneumonia.

Introduction

COVID-19 is caused by a novel viral strain from the family of Coronaviridae (SARS-CoV-2) that primarily infects the respiratory epithelium. Since the appearance of the first case in the latter half of 2019, the COVID-19 pandemic has continued to grow immensely [1,2,3,4]. The emergence of more virulent viral strains has significantly threatened the recently established COVID-19 diagnostic and management strategies [5].

The clinical spectrum of COVID-19 disease ranges from asymptomatic infection to critical disease. Hypoxemia, an indicator of lung involvement, is infrequent in mild cases. However, a diagnostic dilemma could be created in some cases because of the symptoms of hypoxemia being absent (silent hypoxemia) until the late stages [6]. Owing to the high chest X-ray (CXR) positivity rate, even in silent hypoxemia, CXRs are frequently requested to assess lung involvement [7]. However, the subsequent need for intense infection control measures in CT suites, difficulties in mobilizing hypoxic patients, and the involvement of high radiation have reduced the number of chest CT requests in this pandemic [7,8,9].

Severity scores have been used for quantitative and objective estimation of lung involvement and progression [10]. Though several severity scoring systems are available, there is a significant inhomogeneity in the assessment methodologies; some evaluate the area involved, while others focus on infiltrative patterns [7,10,11].

COVID-19 pneumonia CXR infiltrative patterns and their distribution correlated with the disease severity; ground-glass opacities were typical in early or less severe cases, while consolidation was prevalent in critical cases [10]. The patchy peripheral lung opacities identified in

Ceylon Medical Journal 2021; **66:** 168-176

DOI: http://doi.org/10.4038/cmj.v66i4.9507

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progressive stages subsequently spread to involve the entire lung in peak stages [10].

Therefore, we hypothesize that a severity score that assesses both extent involved and infiltrative patterns predict COVID-19 pneumonia severity better than a score based on one of those features. Thus, this study aimed to validate three severity scoring systems to assess COVID-19 pneumonia that evaluate area involved and density patterns, and to identify the most suitable CXR scoring system to predict the mortality.

Methodology

This retrospective study has examined CXRs of confirmed COVID-19 pneumonia patients treated at the Base Hospital of Homagama, Sri Lanka, from 1st December 2020 to 1st February 2021. Ethical clearance was granted by the Ethics Review Committee of the Sri Lanka Medical Association (Protocol No: ERC/21-001).

The study centre admits and manages symptomatic COVID-19 patients with underlying comorbidities. The infection was diagnosed either by a positive COVID-19 Reverse Transcriptase Polymerase Chain Reaction (RT PCR) test or a rapid immunoassay test to detect SARS COV-2 antigen (rapid antigen test). Radiological and clinical features were used to diagnose pneumonia. Relevant socio-demographic, clinical, investigation and outcome details were retrospectively extracted from records. The disease outcomes were defined as recovered and discharged (low clinical severity) or fatal (high clinical severity).

All the CXRs were obtained as anteroposterior (AP) or supine projections using the same portable unit. Observer bias was minimized by evaluating all CXRs at the same Digital Radiography workstation, according to pre-defining CXR signs as per Fleshners glossary [12], and by recording CXR signs with the consensus agreement of Two Radiologists who have been experienced in CXR reporting for more than seven years.

By reviewing the records of all patients (n=301) treated during the study period, two were excluded due to data deficiency and one patient aged less than 18 years was excluded. The CXRs (n=147) with typical COVID-19 pneumonia features belong to eighty-five patients (n=85) were included to assign a severity score (Figure 1).

Chest X-ray severity score

The severity score for each CXR was calculated using three different scoring systems that assessed area and density of lung infiltrate: A score, A and D score, New score. When multiple CXRs were available for a single patient, the CXR with the highest severity score was used to evaluate the association with the outcome.

Area score (A score): The score was calculated using the area involved in the entire lung: score 0 = 0% involvement; 1≤25%; 2=25-50%; 3=50 -75%; 4≥75% area involvement [11]. The patient's total severity score is ranged from 0 to 8. The CXR severity for each patient was defined using the total severity score - mild: 1 to 2; moderate: 3 to 5; severe: 6 to 8.

Area and density score (A and D score): In addition to the area, predominant CXR density pattern was also considered (ground glass or reticular pattern=1; consolidation pattern=2) for severity score calculation. The product of area (obtained as in method 1) and pattern scores was taken as the total score of each lung. The patient's total severity score ranges from 0 to 16 (mild: 1 to 5; moderate: 6 to 10; severe: 11 to 16).

New score: Each lung was divided into three equal zones as described by Borgeshi *et al.* [7]. A severity score was assigned for each zone, considering both area involved (score 0 = no involvement; 1≤25%; 2=25-50%; 3=50-75%; 4≥75% area involvement) and the density of the predominant pattern (ground glass or reticular pattern=1; consolidation pattern=2). The total score of each patient ranges from 0 to 48 (mild - 1 to 16; moderate - 17 to 32; severe - 33 to 48).

Statistical analysis

Once preliminary analysis confirmed the normal distribution, a parametric evaluation was performed. Continuous variables were expressed as means and standard deviations, and categorical variables as modes and percentages. The relationship between groups was evaluated using T-test, Chi-square analysis and binary logistic analysis. A P-value less than 0.05 was considered significant.

The area under the curve analysis was performed to identify the most suitable severity score that predicted the fatal outcome by calculating each system's cut off values. Sensitivity, specificity, positive and negative predictive values were calculated for cut off values. Binary logistic regression analysis was performed to identify the best severity score to predict the fatal patient outcome at the given cut off value.

Results

Table 1 summarizes the demographic characteristics of the cohort. The study included CXRs of 48 men (56.5%) and 37 women (43.5%), aged 63±12.7 years; median 64 years; interquartile range 53 to 72 years. Out of all, 83.5% were older than 50 years. Representing the general ethnic distribution in Sri Lanka, Sinhala ethnic group predominantly (57.6%) represented the study cohort. The case fatality rate of the study cohort was 28.6% (n=24).

Out of all CXRs done during the study period (n= 457), typical COVID-19 pneumonia features were present in 147 (32.2%), while the rest had features of previous lung pathology (n=33; 7.2%); any other comorbidity (n=58; 12.7%) or indeterminate features (n=20; 4.4%).

Table 1. Basic demographic information of the study cohort

Characteristic	*Number (n=85)*	*Percentage*
Age		
30-40 years	4	4.7%
41-50 years	10	11.8%
51-60 years	15	17.6%
61-70 years	30	35.3%
71-80 years	19	22.3%
> 80 years	7	8.2%
Gender		
Male	48	56.5%
Female	37	43.5%
Ethnicity		
Sinhala	49	57.6%
Moore	26	30.6%
Tamil	9	10.6%
Other	1	1.2%
Associated comorbidity present	77	90.59%

Figure 2 depicts the distribution of severity scores in the right and left lungs and each zone. Irrespective of assessment method, the mean scores of right and left lungs were significantly different (A score: T=2.583; p=0.01; A and D score: T=2.134; p=0.034; New score: T=5.586; p=<0.001); the right lung score was higher than the left lung. Similar side related difference was observed in each lung zone as well (upper zones: T=5.49; p<0.001; mid zones: T=4.276; p<0.001; lower zones: T=2.945; p=< 0.001). In each lung, the lower zone severity score was significantly higher than the upper zone (right lung: T=13.63; p=< 0.001; left lung: T=14.88; p=< 0.001).

Tables 2 and figure 3 describe the relationship between the CXR severity scores and the patient outcomes. When assessed with "A scoring system", the mean severity score of recovered patients was lower than the fatal cases: recovered was 4.98±1.5; fatal was 5.91±1.9 (T=3.28; p=0.01). Among the recovered (56.5%) majority had mild or moderate (score less than 5/8) CXR severity grading (fatal cases: 39.7%; T=3.276; p=0.001). Radiographic severity as calculated with "A" scoring system showed a good correlation to the clinical severity (χ^2=6.745; p=0.034; Table 2).

When assessed with "A and D scoring system", the mean severity score of fatal cases was higher than the recovered: fatal cases 10.39±4.7; recovered cases 7.13±3.8 (T=4.48; p=<0.001), while showing a good correlation between radiological and clinical disease severity (χ^2=12.404; p=0.002; Table 2). The majority of recovered (75.2%) had a mild or moderate CXR severity grading (score less than 11/16).

As evaluated with the "New scoring system", mild or moderate CXR grading (<32/48) was reported frequently among the recovered (94.2%) than the fatal cases (80.4%). The mean severity score was significantly higher in fatal cases: recovered was 16.3±9.2; fatal was 22.3±10.9 (T=3.46; p=0.01). The "New" scoring system showed a good correlation to the clinical disease severity (χ^2=10.219; p=0.006; Table 2).

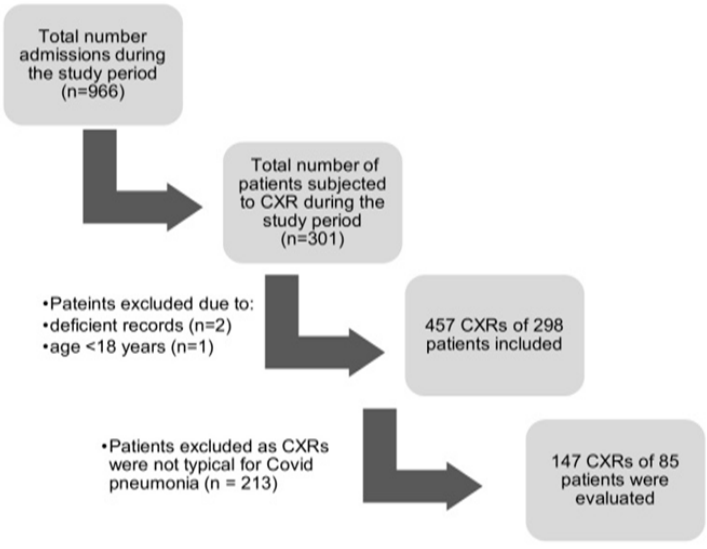


Figure 1. **Flow diagram demonstrating patient selection for the study (CXR-chest Xray).**

When evaluated with "New scoring system", the proportion of patients having severe CXR grading (19.6% fatal cases had CXR severe disease) was agreeable to the true case fatality rates of the study population (28.6%). In contrast, the proportion of patients having severe CXR grades when calculated with other systems were much higher than the actual case fatality: "A scoring system" (69.6%) and "A and D scoring system" (50%).

Predicting the mortality using the severity scoring systems

Figure 4 shows ROC curves of evaluated CXR severity scoring systems as predictors of short term mortality in patients with COVID-19 pneumonia. All three scoring systems were suitable to predict the mortality with a high area under the curve ("A scoring system": AUC=0.685; "A and D scoring system": AUC=0.748; "New scoring system": AUC=0.727; p≤ 0.001). The "A scoring system" showed a sensitivity of 67.4% and specificity of 54.5% at a cut-off point of 5/8 and 40.3% positive predictive value and 78.6% negative predictive value in predicting mortality. At the cut off value of 7/16, the "A and D scoring system" showed a sensitivity of 69.6% and specificity of 61.4% with a 45.1% positive predictive value and 81.6% negative predictive value in predicting mortality. Similarly, with a cut-off point of 18/48, the "New scoring system" showed a sensitivity of 67.4% and specificity of 68.3% with 49.2% positive predictive value and 82.1% negative predictive value.

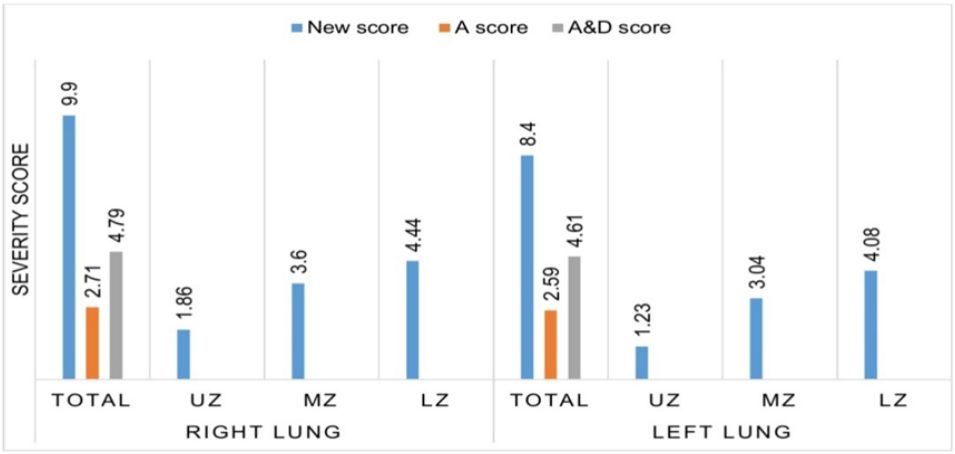


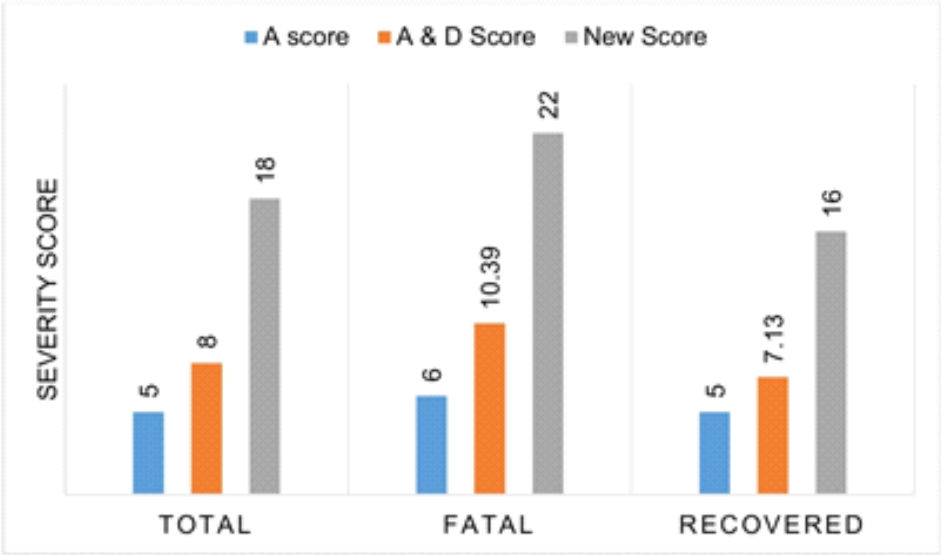
Figure 2. **Distribution of mean severity scores calculated using different scoring systems for each lung.**

(New scoring systems total score is 48; "A" scoring system total score is 8: "A & D" scoring system total score is 16; "New" scoring system assigns a severity score for each lobe while other two systems assign a score for each lung: UZ upper zone; MZ middle zone; LZ lower Zone)

Table 2. Correlation between patient outcome and chest X ray severity score

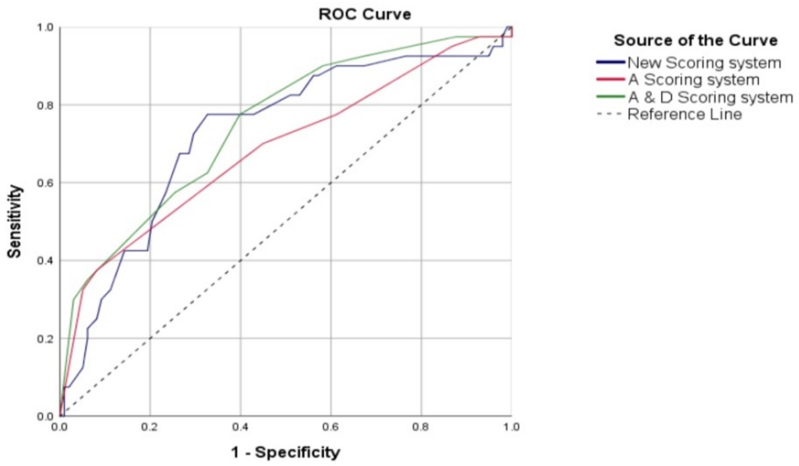
		Fatal	*Recovered*	*Chi-Square*	*P value*
A	Mild (1 to 2)	2 (4.3%)	8 (7.9%)		
Score	Moderate (3 to 5)	12 (26.1%)	46 (45.5%)	6.745	0.034*
	Severe (6 to 8)	32 (69.6%)	47 (46.5%)		
A & D	Mild (1 to 5)	7 (15.2%)	41 (40.6%)		
Score	Moderate (6 to 10)	16 (34.8%)	35 (34.7%)	12.404	0.002*
	Severe (11 to 16)	23 (50%)	25 (24.8%)		
New	Mild (1 to 16)	15 (32.6%)	57 (56.4%)		
Score	Moderate (17 to 32)	22 (47.8%)	38 (37.6%)	10.219	0.006*
	Severe (33 to 48)	9 (19.6%)	6 (5.9%)		

(number of fatal cases = 24, number of X rays evaluated in fatal cases 46; number of recovered cases = 61, number of X rays evaluated in recovered cases 101;*p<0.05)



(The total score of "New" scoring system is 48; the total score of "A" scoring system is 8; the total score "A & D" scoring system is 16; "New" scoring system assigns a severity score for each lobe while other two systems assign a score for each lung:

Figure 3. **Distribution of mean severity scores according to clinical severity when calculated with different scoring system.**



				95% CI	
	AUC	Std.Error	P value	Lower	Upper
New scoring system	0.727	0.049	<0.001	0.631	0.823
A scoring system	0.685	0.053	0.001	0.582	0.789
A & D scoring system	0.748	0.046	<0.001	0.657	0.838

Figure 4. **ROC curves of evaluated severity scoring systems as predictors of short term mortality in patients with Covid pneumonia.**

(AUC – area under the curve)

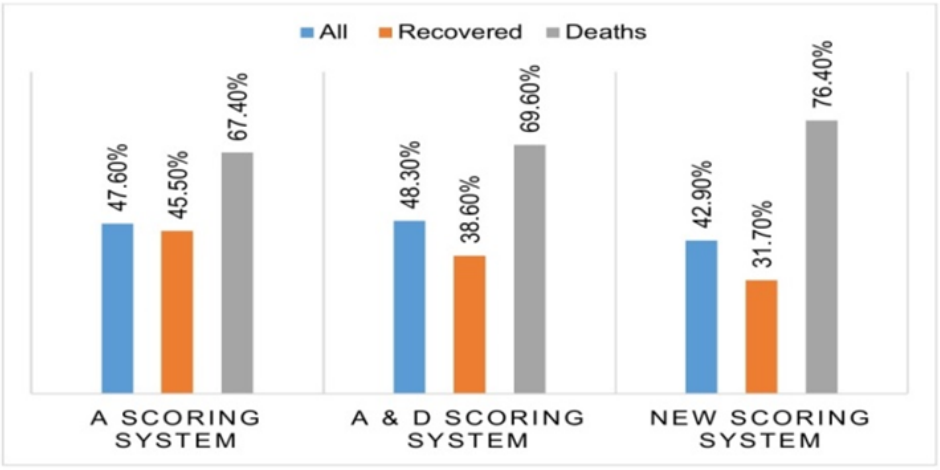


Figure 5. **Distribution of the clinical severity in patients with radiological diagnosed severe disease.**

(radiological severe disease was defiend when the severity score is above the suggested cutoff value for each severity scoring system)

Table 3. The regression analysis of severity scores to predict the death from COVID-19 pneumonia

Severity scoring system	*B*	*S.E.*	*Wald*	*df*	*Exp(B)*	*95% CI*		*P value*
						Lower	*Upper*	
A score	0.133	0.454	0.086	1	1.143	0.469	2.782	0.769
A & D score	0.608	0.477	1.623	1	1.836	0.721	4.678	0.203
New score	1.064	0.508	4.391	1	2.897	1.071	7.836	0.036*

*p<0.05

Figure 5 describes the distribution of the clinical severity in patients with radiological diagnosed severe disease. Though all three systems predicted the fatal cases by indicating a severity score above the cut-off values, the "New severity scoring system" was better at discriminating recovered cases from fatal cases.

The regression analysis taking fatality as the dependent variable has found that the "New severity scoring system" fits the model better than the other two scoring systems (Table 3). A CXR with a severity score of 18 or more obtained using the "New severity scoring system" has predicted mortality in three folds higher than the other two scoring systems (OR: 2.897; CI [1.071-7.8.36]; p=0.036).

Discussion

This study was aimed to validate chest X-ray (CXR) severity scoring systems for their outcome predicting ability in COVID-19 pneumonia. To this end, we introduced three scoring systems based on the lung area involved and the density patterns by considering the whole lung or lung zone for score calculation. Although all tested scoring systems were validated, the "New" scoring system has shown a more contradistinguishing ability.

The CXR is frequently used in COVID-19 pneumonia assessment as it is a cost-effective tool applicable in diverse clinical settings as a triage tool [7]. Quantitative analysis of lung involvement with a CXR severity score had been done with RALE scoring system before the Covid pandemic. The scoring system mentioned has been used to evaluate the severity of pulmonary oedema in acute respiratory distress syndrome (ARDS) for risk stratifications and early interventions while showing an excellent clinical correlation [7,10,13,14].

The RALE system calculates a severity score for each lung quadrant by considering the density of opacity and

extent involved [13]. The "New" scoring system allocates a score for one-third of each lung likewise. Additionally, the "New" system has considered the typical COVID-19 CXR density patterns and their clinical correlations for score calculation. Since ground glass and reticular opacities are features of early or resolving disease (less severe), a lower score (score 1= ground glass or reticular opacities) has been allocated compared with consolidation (score 2=consolidation), which is a feature of either progressive or peak disease [10,11,15,16]. Based on the observed supero-inferior progression of lung involvement in COVID-19 pneumonia [10], dividing the lung into the upper, middle, and lower zones for score allocation is justifiable. All in all, by adopting the methodology of the RALE score, the "New" scoring system is tailor-made to assess the severity of lung involvement in COVID-19 pneumonia.

Though the "New" scoring system shares certain features of the Brixia scoring system, the assessment methods of the two are not similar [7]. When calculating the severity score, the Brixia system ignores the extent of lung involvement, which is a clear indicator of disease severity. Therefore, the Brixia system might be less efficient in providing a clinically significant assessment.

Setiyawati *et al.* and Bhalla *et al.* have described severity scoring systems for COVID-19 pneumonia evaluation [10,14]. Setiyawati *et al.* have considered presence (score 1) or absence (score 0) of opacity and <50% or >50% area involvement by dividing the lung into three zones. Moreover, Bhalla *et al.* have assigned a score for one-third of each lung after considering the involved area. However, these scoring systems have not considered density and area involved as precisely as in the "New" scoring system; they have shown a significant clinical correlation to clinical severity.

Eventhough the CXR severity calculated with "A and D" and "A" systems have shown a positive association with clinical severity, they have overestimated it. In contrast, the "New" system has shown the strongest correlation with the COVID-19 pneumonia outcome. This dissimilarity reflects the methodological differences in score calculation; "A and D" and "A" systems have evaluated a larger lung field while the "New" system assessed one-third of the lung. Our personal experiences in calculating severity scores have pointed out a higher observer variability in an extensive assessment field. Therefore, it is recommended to keep the assessment area reasonably smaller to get more accurate results. When more than one opacity pattern is present in the assessment field, the predominant pattern used for calculation may not indicate the actual density of the entire field. This error can be reduced by assigning a score for a small lung field. However, an assessment field that is too small may produce less accurate results, mainly when the lung is not well expanded due to suboptimal inspiratory effort. Our experiences suggest one-third of the lung field for scoring purposes as the optimum.

The accuracy and reproducibility of a severity scoring system could be enhanced by lowering inter and intra-observer variability. An atlas-based evaluation method, in which the index CXR is compared with a standard image to assign a score, reduces inter and intra-observer variability [17]. Therefore, it is recommended to display standard CXR images in the reporting room that visualize the extent involved and the typical density patterns.

The discernibility of CXR signs is affected by technical factors such as the patient's position, inspiratory effort, motion artefacts, exposure factors (kVp and mAs), and image viewing conditions such as the quality of the image viewer [10,18]. Image viewing conditions particularly deteriorate the detection of subtle signs such as ground-glass opacities [19]. Unlike in standard ward settings, COVID-19 management centres practice various strategies to protect healthcare workers from infection. However, the basic CXR imaging and visualization standards should at least be maintained to obtain accurate results from any severity scoring system. The expertise of the image interpreter is equally vital in producing an accurate severity score. Thus, the image reviewers should be trained to identify subtle signs of COVID-19 pneumonia and distinguish between non-Covid lung disease and Covid lung disease before severity assessment.

Since all scoring systems described in this study and previous studies [10] have shown satisfactory correlation to clinical severity, a semi-quantitative assessment of lung involvement using a severity score is recommended. Serial assessment of CXR severity would be helpful to monitor the progression and treatment responses. For serial monitoring, the same scoring system should be used to avoid confusion between scoring systems.

This study has several strengths. Firstly, we compared and contrasted three scoring systems using suitable statistical methods and identified the most suitable scoring system to indicate clinical severity and outcomes. Secondly, we validated a new scoring system customized for COVID-19 pneumonia assessment while describing its possible clinical uses.

A few limitations of this study are also admitted. We have evaluated the CXR severity only in diagnosed COVID-19 pneumonia patients. Hence, this study does not reveal the scoring systems' ability to discriminate between COVID-19 pneumonia and non-Covid lung diseases. Furthermore, assigning a severity score to patients with severe dyspnoea may not be easy as motion artefacts may degrade images. Additionally, the severity score may not reflect the stage of the disease since both progressive and resolving COVID-19 pneumonia patients may end up with similar severity scores. Thus it may have

practical issues, especially when deciding the need for ICU care. In such instances, interpretation from either the symptomatic day of illness or a serial assessment is suggested. Finally, we have only included CXR positive patients. Among excluded, a proportion may represent false-negative patients who have positive CT features. Therefore, it is recommended to validate CXR severity scoring systems using CT scoring systems.

In conclusion, COVID-19 pneumonia severity, evaluated with chest radiographic severity scoring systems, has correlated significantly with clinical severity and patient outcomes. The scoring system that evaluated zonal lung involvement, using the area involved and density of infiltrates, has predicted the outcome of COVID-19 pneumonia more successfully than other scoring systems. Overall, severity scoring systems provide an innovative, novel method for risk stratification and resource allocation.

Author Contributions

While all authors were involved in all the stages of the research, specific contributions were made as follows. IK involved in conceptualization, study design, data acquisition and management, analysis, interpretation, drafting, and editing manuscript, approval of the final version. BAG involved in conceptualization, data acquisition, critically analyzing manuscript, approval of the final version. NSH – Data acquisition, critically analyzing manuscript, approval of the final version.

Declarations

Ethics approval

Ethical approval was obtained from the Ethics Review Committee of the Sri Lanka Medical Association.

Funding

This work was supported by the Ministry of Health Research Grant: ETR/M/MC/RP/2272/20. NSH has received this grant.

Acknowledgement

We wish to thank the Director, Base Hospital Homagama, and the staff of the Radiology Department for their support. Also the authors like to acknowledge patients involved for their valuable contribution.

Conflict of interest

Authors declare to have no conflict of interest.

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