Journal of Population Therapeutics & Clinical Pharmacology

RESEARCH ARTICLE
DOI: 10.47750/jptcp.2023.30.05.031

Lung ultrasound scoring system vs ROX index as a predictor for progression to the invasive mechanical ventilation in COVID-19 patients

Ibrahim EL-Zoghby[1], Sara Aly[2], Shereen Elgengeehy[3], M. Hamed[4], Karim Mashhour[5]
[1,2,3,4,5]Critical care department, faculty of medicine, Cairo University
***Corresponding author:** Ibrahim EL-Zoghby, Critical care department, faculty of medicine, Cairo University, Email: ibrahim@gmail.com

Submitted: 10 January 2023; Accepted: 09 February 2023; Published: 04 March 2023

ABSTRACT

Background: During the outbreak of the highly contagious Coronavirus disease 19 (COVID19), rapid and simple prognostic tools were needed to support clinical decisions and predict the need of invasive mechanical ventilation. the ROX index, and the lung ultrasound score (LUSS) were proposed to objectively predict patient prognosis in addition to the subjective clinical assessment

Aim: This study aimed to compare lung ultrasound score with ROX index in predicting the need of invasive ventilation in COVID-19 patients requiring advanced oxygen therapy.

Patients and Methods: We studied 50 patients with severe COVID-19 pneumonia in the intensive care unit in the isolated area at Kasr Al-Ainy hospital. Complete Medical history, physical examination and laboratory investigations were obtained on admission. All patients underwent bedside lung ultrasonography scan and LUSS was calculated at the 2nd and the 12th hours, also ROX index was calculated at the 2nd, 6th and 12th hours from initiating the advanced oxygen therapy.

Results: From a total of fifty patients with COVID-19, 56.0% were males, with mean age of 65.98 + 11.68 years, and mortality rate was 68%. The optimal cut off value of the ROX index at (2, 6, 12 hour) is (2.495, 2.675, 3.06) respectively, (p <0.001) with sensitivity 90.9% and specificity 76.5% at the 12 hour. Also the optimal cut off point of LUSS is 25.50 (p <0.001) with sensitivity 93.9% and specificity 88.2% for prediction of the invasive mechanical ventilation.

Conclusion and recommendations: The study concluded that LUSS is more sensitive in predicting the need of invasive mechanical ventilation than ROX index.

Keywords: *COVID-19, Lung ultrasound scoring system , ROX index, HFNC,NIPPV, Invasive mechanical ventilation*

INTRODUCTION

COVID-19 virus is considered as a member of severe acute respiratory syndrome coronavirus and hence renamed as SARS-CoV-2. It is responsible for lower respiratory infection and may lead to acute respiratory distress syndromes. (1)

For those patients with severe respiratory distress, oxygen supplementation via low-flow nasal cannula may be insufficient, and higher flow of oxygen may be needed, and noninvasive modalities (HFNC and NIPPV) may be used rather than proceeding directly to intubation. Identification of requirement and timing for initiation of IMV had been a major challenge.

The ROX index defined as the ratio of oxygen saturation as measured by pulse oximetry/FiO2 to respiratory rate, can help in identifying the patients with low and those with high risk of intubation.(2,3)

Lung ultrasound is an established method in diagnosis of acute respiratory failure. In ARDS, a LUSS has previously been developed to classify the severity of respiratory failure by a 36-point scale based on LUS findings of B-line artifacts (B-lines) and consolidations (4)

A few studies have evaluated LUSS in hospitalized patients with COVID-19. LUS had been found to be a valuable tool in assessment of disease severity and apparently in guiding patients' management, including decisions on mechanical ventilation (5,6). By being a bedside method, LUS has obvious advantages compared to other radiological entities saving hospital resources and reducing viral transmission.

METHODS

From December 2021 to March 2022, 50 patients with severe COVID-19 pneumonia were enrolled in a prospective study conducted in Critical Care Department in Kasr Al-Ainy hospital, Cairo University, Egypt. A consent was obtained from all patients prior to their enrollment in the study together with obtaining an approval from the local ethical committee. The study included patients age > 18 years who suffered severe covid pneumonia with refractory hypoxemia not responding to advanced oxygen therapy, and we excluded pregnant patients and patients with extrapulmonary causes of respiratory failure.

After selection of the patients according to inclusion and exclusion criteria, all patients were subjected to detailed medical history, general and local physical examination, onset of the covid-19 symptoms, routine Laboratory investigations and APACHE II score (Acute Physiology And Chronic Health Evaluation II).

The advanced oxygen therapy was initiated; HFNC was adjusted with flow 40 L/min, and adjusting FiO2 to maintain SpO2 between 92-96%. Vital sings and oxygen saturation were monitored. FiO2 was gradually increased or decreased keeping the target SpO2. Flow was gradually decreased according to the patient's tolerance and reduction of respiratory rate. When patients could not sustain SpO2 or reduce RR using HFNC, they were upgraded to NIPPV. Adjusting the FiO2 with high positive end expiratory pressure (PEEP) to maintain the optimal oxygen saturation.

ROX index was calculated by dividing the oxygen saturation measured by the pulse oximetry over the FiO2 to the respiratory rate at the 2nd, 6th and 12th hours since initiating the advanced oxygen therapy.

LUS scan was done for every patient at the 2nd and the 12th hours of starting the advanced oxygen therapy using A LOGIQ V5 ultrasound GE using a lung preset with a Linear probe: Model L6-12-RS Frequency 6 to 13 MHz and a Curved linear probe: Model C4-RS Frequency 2 to 5 MHz. We used the anterior axillary line and the posterior axillary line as boundaries to divide each side of the chest wall to 3 regions (anterior, lateral and posterior regions) to achieve a total 6 regions of scanning as shown in figure (1). In addition to dividing each lung into 3 regions we use a transverse line connecting both nipples to divide the lung into upper and lower lung fields to achieve 12 regions.

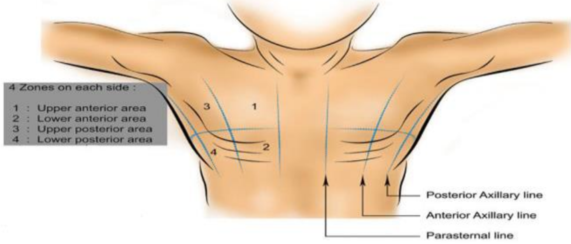

FIG. 1: Anatomical reference lines of the lung ultrasonography protocol (7)

Scoring of each region was performed according to the lung ultrasound scoring system. LUSS is the most frequently used score in the ICU to distinguish the four steps of progressive loss of aeration (8,9). It was calculated as the sum of the points ranging from 0-36.

TABLE 1: The lung-ultrasound scoring system:

Points for each lung zone	Degree of lung aeration	Pattern
0 points	Normal	Presence of lung sliding with horizontal A lines or B lines ≤2
1 points	Moderate loss	Multiple well-defined and spaced B lines, one to three or more well-separated B-lines emerged from the pleural line covering ≤50% of the region
2 points	Severe loss	Multiple coalescent vertical B lines covering >50% of the region emerged from the pleural line.
3 points	Complete loss	Lung consolidation

Fig. (2) normal thickness of the pleural line with multiple A lines (score zero)

Fig. (3) thickned and irregular pleural lines. More than 2 discrete B lines per intercostal space (score 1)

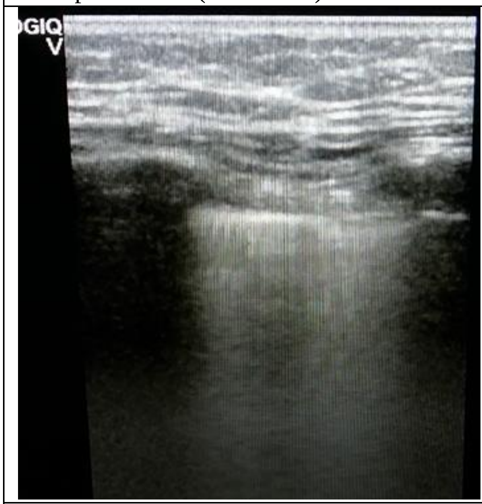

Fig. (4) Thickened irregular pleural lines with multiple coalescent B lines. (Score 2).

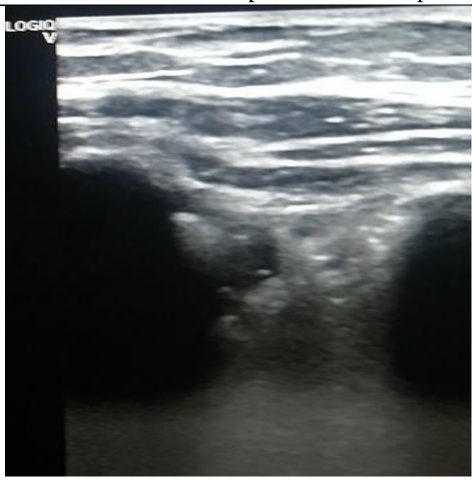

Fig. (5) Irregular and disrupted pleural lines with large consolidations (tissue like pattern) (score 3).

Invasive mechanical ventilation was initiated when a patient's status deteriorated; respiratory rate > 35 breaths/min, obvious accessory respiratory muscle activity, abdominal paradoxical breathing, inability to obtain saturation >93% with FiO2 >80%, progressive increase in PaCO2 or hemodynamic instability.

We aimed to compare lung ultrasound score with ROX index in predicting the need of invasive ventilation in COVID-19 patients requiring advanced oxygen therapy.

Statistical Analysis

Data were coded and entered using the statistical package for the Social Sciences (SPSS) version 28 (IBM Corp., Armonk, NY, USA). Data was summarized using mean and standard deviation for normally distributed quantitative variables or median and interquartile range for non-normally distributed quantitative variables and frequencies (number of cases) and relative frequencies (percentages) for categorical variables. Comparisons between groups were done using unpaired t test in normally distributed quantitative variables while non-parametric Mann-Whitney test was used for non-normally distributed quantitative variables(10). For comparing categorical data, Chi square (x2) test was performed. Exact test was used instead when the expected frequency is less than 5 (11). Correlations between quantitative variables were done using Spearman correlation coefficient (12). ROC curve was constructed with area under curve analysis performed to detect best cutoff value of LUS and ROX for detection of outcome. P-values less than 0.05 were considered as statistically significant.

RESULTS

Our study was conducted on fifty patients diagnosed with severe COVID-19 pneumonia. The mean age of the patients in our study was 65.98 + 11.68 years, 56% of the population were males, the mean Body Mass Index (BMI) was 28.32 in males and 30.90 in females and the most common comorbidities were diabetes (62%) followed by hypertension (46%) and cardiac diseases (28%). Most of the population was dependent on HFNC (70%), and 30% on NIPPV. The mean duration of the advanced oxygen support was 6.42 + 2.57 days. Failure of advanced oxygen therapy ended up with invasive mechanical ventilation, where 66% of the population required intubation and mechanical ventilation for which mortality rate was 100%. The mean duration of the ICU stay was 11.66 + 3.70 days. (Table 2)

TABLE 2: The baseline characteristics:

Age		65.98 ±11.68
Gender	Male	28 (56%)
	Female	22 (44%)
BMI	Male	28.32
	Female	30.90
Type of initial oxygen Support	HFNC	35 (70%)
	NIPPV	15 (30%)
Duration of initial oxygen support		6.42±2.57
Mechanical ventilation	Intubated	33 (66%)
	Non intubated	17 (34%)
Mechanical Ventilation duration		3.70±3.28
APACHE score	Survived	16.59±2.69
	Not survived	16.69±2.50
Outcome	Survived	17 (34%)
	Non-survived	33 (66%)
ICU Stay		11.66±3.70

The mean value of ROX index among the whole population was 2.54, 2.67 and 2.93 at 2, 6 and 12 hours, respectively from initiating the advanced oxygen therapy. ROX index showed significant relationship with mechanical ventilation among the patients using the advanced oxygen therapy. The mean values of ROX index among the intubated patients at 2, 6 and 12 hours were (2.42), (2.57) and (2.71), respectively since starting the advanced oxygen therapy ($p < 0.001$). The ROX index showed higher results among the non-intubated patients with mean values (2.79), (2.90) and (3.34) at 2, 6 and 12 hours, respectively, table (3).

ROX index showed inversely proportional relationship with mechanical ventilation duration, the lower the ROX index, the longer the duration, table (3).

ROX index at different times could provide acceptable predictors for the need of mechanical ventilation and mortality. ROC curve showed that ROX12 is the best predictor for mechanical ventilation and mortality with cutoff point 3.060 (AUC 0.903; sensitivity = 91.2%, specificity = 81.3%), ROX2 and ROX6 predict also mechanical ventilation and mortality with (AUC 0.812; sensitivity = 64.7%, specificity = 81.3%) and (AUC 0.817; sensitivity = 76.5%, specificity = 75%), respectively, table (3), figure (6).

TABLE 3: ROX index versus LUSS:

		ROX Index			LUSS	
		ROX 2	ROX 6	ROX 12	LUSS 2	LUSS 12
Whole population		2.54±0.32	2.67±0.32	2.93±0.48	26±2.78	26±2.78
Type of initial oxygen support	HFNC	2.50±0.33	2.60±0.33	2.89±0.51	26.11±2.77	26.11±2.77
	NIPPV	2.62±0.29	2.84±0.23	3.02±0.42	25.73±2.89	25.73±2.89
Mechanical ventilation	Yes	2.42±0.19	2.57±0.21	2.71±0.31	27.41±1.65	27.41±1.65
	No	2.79±0.41	2.90±0.40	3.34±0.46	23±2.28	23±2.28
	P value	< 0.001	< 0.001	<0.001	< 0.001	< 0.001
MV duration	Correlation Coefficient	0.439	0.424	0.473	0.565	0.565
	P value	0.001	0.002	<0.001	<0.001	<0.001
Prediction of MV & mortality	AUC	0.812	0.817	0.903	0.961	0.961
	P value	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001
	Cut off	2.505	2.675	3.060	25.50	25.50
	Sensitivity %	64.7%	76.5%	91.2%	91.2%	91.2 %
	Specificity %	81.3%	75%	81.3%	87.5%	87.5%

In our study, the number of the affected lung areas did not show much difference, where the mean value of LUS score was 26 points at both 2 and 12 hours. When using either HFNC or NIPPV and the lung ultrasound score didn't vary after 12 hours, ($p = 0.662$). The mean value of LUSS was 26.11 points using HFNC and 25.73 points using NIPPV. The mean value of the LUSS among the intubated patients was higher than the non-intubated patients with significant ($p < 0.001$). The mean LUSS was 27.41 points among the intubated patients and 23.00 points among the non-intubated patients. The LUSS after 12 hours had no significant difference than the LUSS after 2 hours in predicting the need of mechanical ventilation, table (3). LUSS shows directly proportional relationship with the mechanical ventilation duration, the higher the LUSS, the longer the duration of mechanical ventilation. The mean value of the LUSS among the non-survived patients was higher than the survived patients with significant ($p < 0.001$). The mean LUSS was 27.41 points among the non-survived patients and 23.00 points among the survived patients. The LUSS after 12 hours had no significant difference than the LUSS after 2 hours in predicting mortality.

LUS score proved a high sensitivity and specificity in predicting the need of mechanical ventilation and mortality. ROC curve for LUSS showed that the optimal cutoff point for the need of mechanical ventilation is 25.5 (AUC 0.961; sensitivity = 91.2%, specificity = 87.5%), figure (7). Applying the LUSS after 12 hours since using the advanced oxygen therapy didn't provide significant difference in predicting the need of mechanical ventilation, as it showed the same results as LUSS at 2 hours.

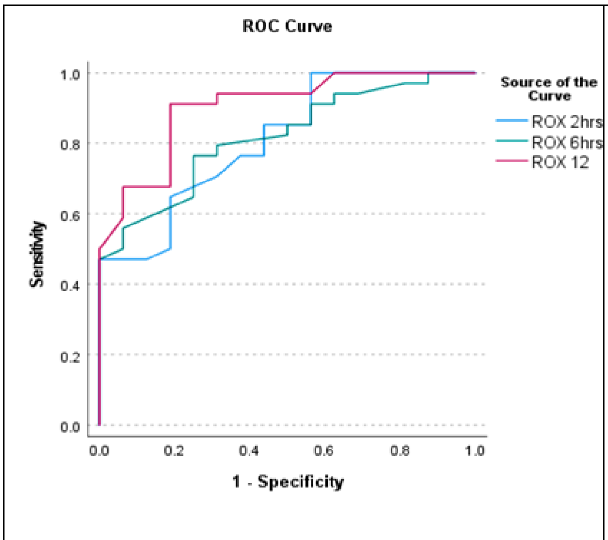

Fig. (6) ROC curve for ROX index as a predictor for MV and mortality

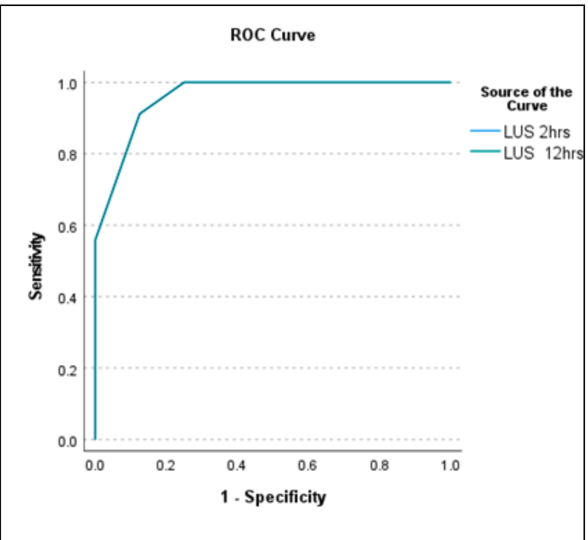

Fig. (7) ROC curve for LUS score as predictor for mortality

DISCUSSION

Bedside lung ultrasound has emerged as a useful and non-invasive tool to detect lung disease and monitor changes in patients with (COVID-19). We aimed to investigate the prognostic value of the LUS score to assess the need of invasive mechanical ventilation in moderate to severe COVID-19 pneumonia in comparison to ROX index.

Mortality rate in our study was significantly high. Sixty-six percent of the total population was mechanically ventilated after failure of advanced oxygen support with mortality rate 100%. This was explained by the narrow spectrum of the group study, the severity of the disease (all the patients had severe COVID-19 pneumonia with respiratory failure), the risk factors and complication related to the mechanical ventilation (pneumothorax and secondary bacterial infection). In agreement with our study, The Lancet provided insight into the clinical course and mortality risk for adults with COVID-19 that was severe enough to require hospitalization. They reported findings from 191 patients with COVID-19 from Wuhan during the first month of the outbreak. The mortality rate was 28%. 16% of the patients required IMV, with mortality rate 97%. In another report from Wuhan mortality was 62% among critically ill patients with COVID-19 and 81% among them required IMV (13).

ROX index was first applied on non-COVID-19 patients with acute respiratory failure to predict the need of invasive mechanical ventilation. ROX Index < 4.88, measured at 12 h after HFNC onset, was related to a higher risk of intubation (p <0.002; AUC=0.74) (2).

In our study, we used ROX index to predict failure of advanced oxygen therapy (NIPPV & HFNC) in patients with acute hypoxemic respiratory failure due to COVID19 pneumonia, during the first 24 hours of treatment. The ROC analysis identified the ROX12 as the best predictor for intubation and mortality with cutoff value 3.060 (p <0.001; AUC=0.903, sensitivity 91.2%, specificity 81.3%). We might think that ROX12 may delay intubation, but we saw that all patients in our study were intubated not before 72 hours.

In agreement with our study, a prospective observational study suggested that the ROX index was a valuable predictive parameter among patients with severe COVID-19 pneumonia. It was found that the ROX index values <3.85 measured in the first 12 hours after HFNC initiation were associated with a higher rate of intubation and death (14). Also a retrospective study concluded that the ROX12 index has a positive predictive value (59.4%) using threshold of <3.85 for COVID-19 patients predicting invasive mechanical ventilation (15).

We concluded that, the mean LUS score was 27.41 points among the intubated patients and 23.00 points among the non-intubated patients. The optimal cutoff point for the need of invasive mechanical ventilation is 25.50 points, (p <0.001; AUC=0.966; sensitivity 93.9%, specificity 88.2%). The follow up LUS score after 12h did not vary significantly in the number of the affected lung areas with the same mean LUS score among the intubated and the non-intubated patients. In agreement with our study, a retrospective study showed that LUSS was significantly higher in the mechanically ventilated group 33 vs 25.5 points (p = 0.047). The ROC curve of the LUSS showed a cut off score of 32 points (specificity of 89%, sensitivity of 57%) in diagnosing refractory respiratory failure among patients and the need of invasive mechanical ventilation (9).

Our study was supported by other studies; in a prospective cohort study, LUS score >22 points was a good predictor of ICU admission and mortality (AUC= 0.693; p =0.023, sensitivity 76.9%, specificity 62.1%). The number of lung areas affected did not vary significantly after 72 hours of admission (16). Also in a prospective observational study, the performance of the lung ultrasound was evaluated to determine the short-term outcomes of COVID-19 patients admitted to the intensive care unit. The median LUS score at ICU admission was 20.8±6.1; at day 5, it was 27.6±5.5 and at day 10, 29.4±5.3 (p =0.007). As clinical condition deteriorated (according to the requirement for invasive mechanical ventilation), the LUS score increased. The LUS score was also a good predictor of mortality (p <0.001) (17). Another study correlated the LUS score with the need for invasive mechanical ventilation and is a strong predictor of mortality. The median baseline LUSS was 15 points. Clinical deterioration was associated with follow up LUSS (p = 0.0009). The optimal cut off point for invasive mechanical ventilation was 18 (sensitivity 62%, specificity 74%) (18).

It was found that patients with the highest LUS score were more likely to have higher incidence of respiratory failure, ARDS, mechanical ventilation, and higher mortality. Patients with a high LUS score had a higher rate of bilateral lung involvement; the most common findings were thickening of the pleural line with pleural line irregularity, B lines in a variety of numbers and patterns, consolidations and occasionally pleural effusions.

CONCLUSION

LUS-score had a strong diagnostic value for identification of requirement of invasive mechanical ventilation and mortality in patients with severe COVID-19 pneumonia.

Comparing LUS with ROX index, LUS is more accurate in predicting the need of invasive mechanical ventilation and mortality after using the advanced oxygen support.

ACKNOWLEDGEMENTS

We appreciate the great help of the whole team in critical care department, Cairo University for their great help & support.

REFERENCES

1. Y. W, Y. W, Y. C, Q. Q. Unique epidemiological and clinical features of the emerging 2019 novel coronavirus pneumonia (COVID-19) implicate special control measures. J Med Virol. 2020;
2. Roca O, Messika J, Caralt B, García-de-Acilu M, Sztrymf B, Ricard JD, et al. Predicting success of high-flow nasal cannula in pneumonia patients with hypoxemic respiratory failure: The utility of

the ROX index. J Crit Care. 2016;35.

3. Suliman LA, Abdelgawad TT, Farrag NS, Abdelwahab HW. Validity of rox index in prediction of risk of intubation in patients with covid-19 pneumonia. Adv Respir Med. 2021;89(1).
4. Bouhemad B, Mongodi S, Via G, Rouquette I. Ultrasound for “lung monitoring” of ventilated patients. Vol. 122, Anesthesiology. 2015.
5. Deng Q, Zhang Y, Wang H, Chen L, Yang Z, Peng Z, et al. Semiquantitative lung ultrasound scores in the evaluation and follow-up of critically ill patients with COVID-19: a single-center study. Acad Radiol. 2020;27(10).
6. de Alencar JCG, Marchini JFM, Marino LO, da Costa Ribeiro SC, Bueno CG, da Cunha VP, et al. Lung ultrasound score predicts outcomes in COVID-19 patients admitted to the emergency department. Ann Intensive Care. 2021;11(1).
7. Niyogi SG, Kumar B, Puri GD, Negi S, Mishra AK, Singh Thingnam SK. Utility of Lung Ultrasound in the Estimation of Extravascular Lung Water in a Pediatric Population—A Prospective Observational Study. J Cardiothorac Vasc Anesth. 2022;36(8).
8. Soummer A, Perbet S, Brisson H, Arbelot C, Constantin JM, Lu Q, et al. Ultrasound assessment of lung aeration loss during a successful weaning trial predicts postextubation distress. Crit Care Med. 2012;40(7).
9. Zhao L, Yu K, Zhao Q, Tian R, Xie H, Xie L, et al. Lung Ultrasound Score in Evaluating the Severity of Coronavirus Disease 2019 (COVID-19) Pneumonia. Ultrasound Med Biol. 2020;46(11).
10. Chan YH. Biostatistics 102: Quantitative Data - Parametric & Non-parametric Tests. Singapore Med J. 2003;44(8):391–6.
11. Chan YH. Biostatistics 103: Qualitative Data - Tests of Independence. Vol. 44, Singapore Medical Journal. 2003. p. 498–503.
12. Chan. Biostatistics 104: correlational analysis. Singapore Med J. 2003;
13. Weiss P, Murdoch DR. Clinical course and mortality risk of severe COVID-19. Vol. 395, The Lancet. 2020.
14. Celejewska-Wójcik N, Polok K, Górka K, Stachura T, Kania A, Nastałek P, et al. High-flow nasal oxygen therapy in the treatment of acute respiratory failure in severe COVID-19 pneumonia: A prospective observational study. Polish Arch Intern Med. 2021;131(7–8).
15. Myers LC, Mark D, Ley B, Guarnieri M, Hofmeister M, Paulson S, et al. Validation of Respiratory Rate-Oxygenation Index in Patients With COVID-19-Related Respiratory Failure. Crit Care Med. 2022;50(7).
16. Rubio-Gracia J, Giménez-López I, Garcés-Horna V, López-Delgado D, Sierra-Monzón JL, Martínez-Lostao L, et al. Point-of-care lung ultrasound assessment for risk stratification and therapy guiding in COVID-19 patients: A prospective noninterventional study. Eur Respir J. 2021;58(3).
17. Sosa FA, Matarrese A, Saavedra S, Osatnik J, Roberti J, Oribe BT, et al. Lung ultrasound as a predictor of mortality of patients with covid-19. J Bras Pneumol. 2021;47(4).
18. Lichter Y, Topilsky Y, Taieb P, Banai A, Hochstadt A, Merdler I, et al. Lung ultrasound predicts clinical course and outcomes in COVID-19 patients. Intensive Care Med. 2020;46(10).