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Original Research Article

Predictors of failure of non-invasive ventilation in severe COVID 19 patients

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ABSTRACT

Background: Respiratory oxygenation index (ROX index) is a simple parameter that uses bedside parameters like respiratory rate and peripheral oxygen saturation. It has been extensively evaluated to predict success of HFNC in patients with pneumonia and found beneficial in predicting HFNC failure. However, there are very few literatures are available to establish the efficacy of ROX index in predicting NIV success. The aim of this study was to determine whether the ROX Index could predict NIV therapy success in patients with AHRF due to SARS-CoV-2 pneumonia.
Methods: After obtaining approval and clearance from the institutional ethics committee of BMCRI, patients who were admitted in Victoria Hospital intensive care unit with acute respiratory failure due to COVID-19 who were initiated on NIV or CPAP based on clinician decision during the study period of April 2020 – July 2021 were included.
Results: The optimal cut-off value of ROX index for predicting ventilatory requirement according to the maximum Youden index was ≤3.93. This cut-off value showed a sensitivity of 89.83% and a specificity of 92.86%, and the AUC was 0.965 (95% CI 0.909 to 0.992, P<0.0001).
Conclusions: When compared between ROX index, SPO2 at Room air and CT Score, it was observed that ROX index had the highest, AUROC, sensitivity, and specificity. This indicates that ROX index can be used as a predictive variable for NIV failure or success.

Keywords: NIV, COVID-19, ROX index

INTRODUCTION

Coronavirus disease 2019 (COVID-19), caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus, is a novel viral infection that is fast spreading over the world, and the World Health Organization declared it a pandemic three months after it first appeared.[1] In order to cope with and manage these patients, several hospitals were obliged to prepare and develop guidelines for the healthcare staff to follow. COVID-19 individuals present a wide range of symptoms, including fever, cough, fatigue, sputum production, and shortness of breath.[3] Approximately 14% of patients develop a severe form of COVID-19, necessitating hospitalisation, and the percentage of patients requiring ICU care ranges from 5% to 32%.[4-6]

Patients over the age of 65, as well as those with chronic underlying conditions, are more likely to develop severe illness and complications such as acute hypoxemic respiratory failure (AHRF), acute respiratory disease syndrome (ARDS), sepsis, septic shock, and kidney and

cardiac failure, which necessitate intensive care unit (ICU) treatment and supportive respiratory therapy.[7] Non-invasive ventilation (NIV) and high-flow nasal cannula are the most often used treatments for acute respiratory insufficiency (HFNC). The NIV has been used to treat AHRF caused by SARS-CoV-2 that is unresponsive to normal oxygen therapy, according to new guidelines for the respiratory care of SARS-CoV-2 illness.[2,3,9] However, data on the safety and efficacy of NIV and HFNC in these patients is inadequate, and there are considerable concerns regarding the spread of infection among healthcare professionals caring for patients in SARS-CoV-2-infected locations. In addition, a significant number of patients fail on NIV and require intubation and mechanical ventilation.

The respiratory oxygenation index (ROX index) is a basic metric that takes into account bedside characteristics such as respiratory rate and peripheral oxygen saturation. The ROX index is a ratio of pulse oximetry oxygen saturation/fraction of inspired oxygen to respiratory rate. It has been widely studied to predict the success of HFNC in patients with pneumonia and has been demonstrated to be useful in predicting HFNC failure.[10]

Given the overwhelming volume of admissions, early triaging and identification of the critically ill is vital in managing COVID-19 infection. The ROX index's simplicity makes it a good metric for predicting outcomes in NIV patients. However, there is a paucity of evidence to support the efficacy of the ROX index in predicting NIV success.

The purpose of this study was to see if the ROX Index could predict the efficacy of NIV therapy in patients with AHRF caused by SARS-CoV-2 pneumonia.

Objectives of the study

To determine predictors of NIV failure in patients with ARF due to severe SARS-CoV-2 pneumonia.

METHODS

A retrospective cross-sectional study conducted in Victoria Hospital. After obtaining approval and clearance from the institutional ethics committee of BMCRI, patients who were admitted in Victoria Hospital intensive care unit with acute respiratory failure due to COVID-19 who were initiated on NIV or CPAP based on clinician decision during the study period of April 2020 – July 2021 were included. Medical records of those admitted patients were verified from the medical Records Section of the Victoria Hospital. Those fulfilling the inclusion criteria were included in the study. From the medical records, case history, all investigations, treatment, and course in hospital were compiled in Microsoft excel and analyzed using IBM- Statistical package for social sciences (SPSS) version.[24]

Inclusion criteria

Patients above 18 years of age. Patients willing to give informed consent. Patients with moderate or severe COVID 19 pneumonia as per NIH COVID 19 treatment guideline who were treated with NIV.

Exclusion criteria

Patients with any formal contraindications for NIV. Patients who expired within 60 mins of initiating NIV. Patients with immediate indication for invasive mechanical ventilation. Patients with mild COVID 19 infections.

RESULTS

Between April 2021 and June 2021, 101 patients with moderate or severe COVID 19 pneumonia and treated with NIV, were enrolled. From the included patients 59 (58%) patients died.

Table 1: Characteristics of the subjects.

		Recovered (n=42)		NIV Failure (n=59)		
		Count	**Column N %**	**Count**	**Column N %**	**P value**
Age (in years)	20-29	1	2.4%	1	1.7%	0.000
	30-39	7	16.7%	8	13.6%	
	40-49	10	23.8%	12	20.3%	
	50-59	14	33.3%	17	28.8%	
	60-69	3	7.1%	11	18.6%	
	70-79	6	14.3%	7	11.9%	
	80-89	1	2.4%	3	5.1%	
Sex	Female	18	42.90%	21	35.60%	0.000
	Male	24	57.10%	38	64.40%	0.000
Comorbidities	DM	4	9.50%	7	11.90%	0.000
	HTN	4	9.50%	5	8.50%	
	Multiple comorbidities	31	73.80%	43	72.90%	
	None	3	7.10%	4	6.80%	

Table 2: Clinical findings of the subjects.

	Recovered (N=42)		NIV Failure(N=59)		
	Mean	**SD**	**Mean**	**SD**	**P value**
FiO2	71.33	16.10	95.17	5.65	0.000
SPO2 AT RA	80	6	70	7	0.000
SpO2	91	3	90	4	0.019
PR	103	11	116	8	0.000
Systolic	125	13	124	17	0.000
Diastolic	76	13	78	15	0.000
RR	25	3	28	4	0.000
P/F ratio	91.10	37.61	73.79	49.57	0.000
Ddimer	1723	1809	2613	1888	0.000
CRP	166.40	150.85	338.01	331.50	0.000
LDH	529.26	257.56	960.53	686.28	0.000
Ferritin	861	634	1006	738	0.000
Hb	12.4	2.2	18.5	34.6	0.000
TC	11223	5771	12459	6608	0.000
ROX	5.239	1.156	3.281	0.604	0.000
DAYS IN ICU	8	2	10	4	0.000

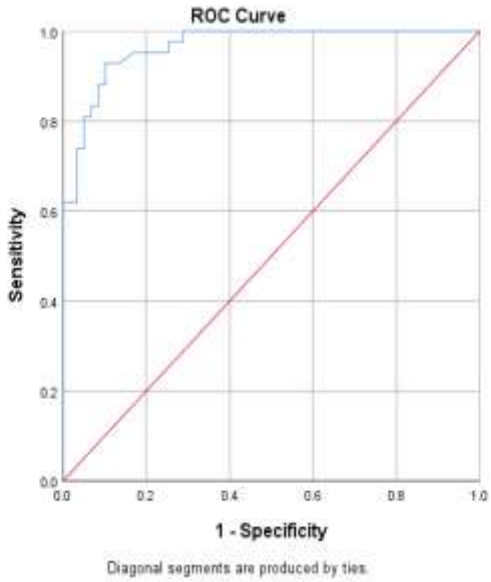

Figure 1: ROC curve – ROX index versus outcome.

Table 1 shows the patients' characteristics. Most of the study patients were male (61%). The mean age of the subjects was 54±14 years. Comorbidities were present in 33 (78.6%) subjects who recovered and in 44 (74.6%) subjects who had NIV failure. Significant association was found between gender, and presence of comorbidities and NIV failure.

It was observed that in the group that had NIV failure, the mean FiO2 was significantly higher (95.17±5.65, p=0.000). SPO2 at room air and SPO2 were significantly lower in the NIV failure group. Mean Pulse Rate (116±8 bpm) and respiratory rate (28±4 cpm) were scientifically higher in the group with NIV failure. Average D-dimer (2613±1888 ng/ml), CRP (338.01±331.50 microgm/ml), LDH (960.53±686.28 units/L), Ferritin (1006±738 microgm/L), Hb (18.5±34.6 g/dl), and TC (12459±6608 cells/cumm) was significantly higher in the group with NIV failure. Average number of days in ICU (10±4 days) was significantly more in the group with NIV failure. (Table 2)

The optimal cut-off value of ROX index for predicting ventilatory requirement according to the maximum Youden index was ≤3.93. This cut-off value showed a sensitivity of 89.83% and a specificity of 92.86%, and the AUC was 0.965 (95% CI 0.909 to 0.992, p<0.0001). (Table 3, Figure 1)

Table 3: Area under the ROC curve (AUC).

Area under the ROC curve (AUC)	0.965
Standard Error a	0.0147
95% Confidence interval b	0.909 to 0.992
z statistic	31.630
Significance level P (Area=0.5)	<0.0001

[a] DeLong et al., 1988. [b] Binomial exact

Table 4: Youden index.

Youden index J	0.8269
Cut off	≤3.93
Sensitivity	89.83
Specificity	92.86

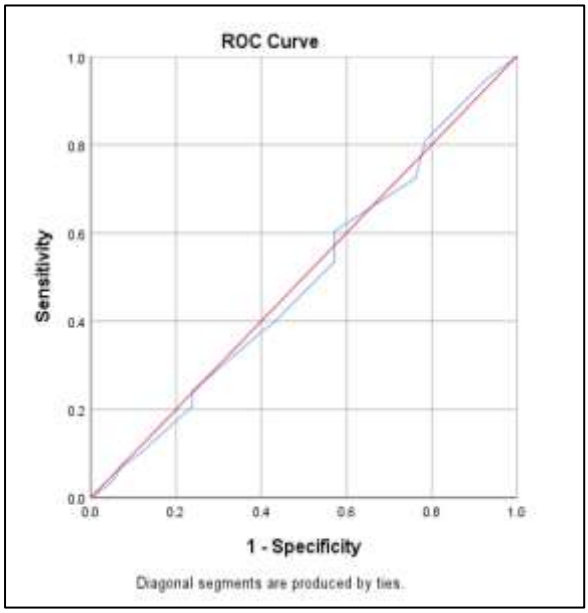

Figure 2: ROC curve – CT score versus outcome.

Table 5: Area under the ROC curve (AUC).

Area under the ROC curve (AUC)	0.778
Standard Error [a]	0.0471
95% Confidence interval [b]	0.684 to 0.855
z statistic	5.908
Significance level P (Area=0.5)	<0.0001

[a] DeLong et al., 1988. [b] Binomial exact

The optimal cut-off value of ROX index for predicting ventilatory requirement according to the maximum Youden index was ≤3.93. This cut-off value showed a sensitivity of 89.83% and a specificity of 92.86%, and the AUC was 0.965 (95% CI 0.909 to 0.992, p<0.0001). (Table 3, Figure 1)

The optimal cut-off value of SPO2 AT room air for predicting ventilatory requirement according to the maximum Youden index was ≤77. This cut-off value showed a sensitivity of 81.36% and a specificity of 80.95%, and the AUC was 0.883 (95% CI 0.804 to 0.938, p<0.0001).

Table 6: Youden index.

Youden index J	0.4361
Cut Off	>17
Sensitivity	72.88
Specificity	70.73

The optimal cut-off value of CT score for predicting ventilatory requirement according to the maximum Youden index was >17. This cut-off value showed a sensitivity of 72.88% and a specificity of 70.73%, and the AUC was 0.778 (95% CI 0.684 to 0.855, p<0.0001).

When compared between ROX index, SPO2 at room air and CT score, it was observed that ROX index had the highest, AUROC, sensitivity, and specificity. This indicates that ROX index can be used as a predictive variable for NIV failure or success.

DISCUSSION

The population was dominated by men (61 percent) and the elderly. According to a prior study, male gender and older age are related with severe COVID-19.[11] In the current study, 76 percent of patients had at least one comorbidity, which is significantly higher than in previous investigations.[4,5,12] However, in other investigations, heart disease and cancer were found to have a substantial correlation with COVID 19 mortality. In our analysis, having many comorbidities was associated with a higher risk of death.

The ROX index measured in this study could be utilised as a diagnostic of NIV failure. Several studies have found that the SpO2/FiO2 ratio is a reliable predictor of ARDS severity and can help guide the care of critically ill patients who require ventilatory assistance.[13-16] We discovered a strong correlation between decreased SPO2 at room air and NIV failure in this investigation.

To our knowledge, the ROX index has rarely been studied as a predictor of NIV performance in COVID or non-COVID patients. The ROX index was derived in the current study while the patients were breathing room air by dividing SpO2/0.21 by RR prior to the commencement of any ventilatory support, and a value of 3.93 is significantly predictive of early NIV failure. Even after controlling for age, a low ROX index remained independently related with early NIV failure. A recent study found that a ROX index of 5.4 assessed during the first 4 hours of HFNC commencement could be utilised as a predictor of the need for invasive mechanical ventilation.[17]

According to the highest Youden index, the ideal cut-off value of CT SCORE for predicting ventilatory need in the current investigation was >17. The sensitivity was 72.88 percent, the specificity was 70.73 percent, and the AUC was 0.778 for this cut-off value. Mukhtar (2020) discovered that the best CT score for predicting the need for mechanical ventilation was 13. (sensitivity 80 percent, specificity 73 percent, AUC 0.9).[18] In another study, Mahdjoub discovered that the best CT score to predict a bad 5-day outcome was 13. (sensitivity 80 percent, specificity 85.2 percent, AUC 0.853).[19]

According to the maximal Youden index, the ideal cut-off value of SPO2 at Room Air for estimating ventilatory need was 77 percent in this investigation. The sensitivity was 81.36 percent, the specificity was 80.95 percent, and the AUC was 0.883 for this cut-off value. According to Mukhtar, the ideal cut-off value of SpO2 for forecasting ventilatory need based on the highest Youden index was 78%. This cut-off value had a sensitivity of 70% and a specificity of 100%, with an AUC of 0.9.16.

The pandemic pattern of COVID-19 caused a severe lack of medical supplies in several nations, raising the fatality rate.[18] As a result, it is critical to prioritise patients as soon as possible and to identify the sickest patients who should be referred to better equipped institutions. It is also recommended that this triage be carried out utilizing the simplest and most cost-effective means possible in a setting with limited resources.

Limitations

This study has some drawbacks. First, this was a pandemic study, and the critical nature of the pandemic prevented us from obtaining more detailed clinical information, such as tidal volume during NIV; higher tidal values could be associated with an increased risk of self-inflicted lung injury and worsen ventilator-induced lung injury. Second, we exclusively enrolled individuals who were admitted during a brief time period when medical services were overburdened by the COVID-19 outbreak. The median time from symptom onset to hospitalisation or ICU admission, as well as the use of respiratory assistance, may differ after a pandemic or in various countries. Third, agitation and intolerance to masks may have had predictive implications in assessing NIV failure in comparison to the assessed parameters (e.g., ROX index). These data, however, were not available in our investigation.

CONCLUSION

In conclusion, ROX index in patients with COVID-19 at hospital admission is a reliable tool in predicting the outcome of patients. A baseline ROX index ≤3.93% could predict the need for MV support with a sensitivity of 89.83% and specificity of 92.86%.

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Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. World Health Organization. Diagnostics, therapeutics, vaccine readiness, and other health products for COVID-19: a module from the suite of health service capacity assessments in the context of the COVID-19 pandemic: interim guidance, 20 October 2020. World Health Organization. 2020.
2. Lazzeri M, Lanza A, Bellini R, Bellofiore A, Cecchetto S, Colombo A et al. Respiratory physiotherapy in patients with COVID-19 infection in acute setting: a Position Paper of the Italian Association of Respiratory Physiotherapists (ARIR). Monaldi Archives for Chest Disease. 2020;90(1).
3. Righetti RF, Onoue MA, Politi FV, Teixeira DT, Souza PN, Kondo CS et al. Physiotherapy care of patients with coronavirus disease 2019 (COVID-19)-a Brazilian experience. Clinics. 2020;75.
4. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. The lancet. 2020;395(10223):497-506.
5. Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX et al. Clinical characteristics of coronavirus disease 2019 in China. New England J Med. 2020;382(18):1708-20.
6. Grasselli G, Pesenti A, Cecconi M. Critical care utilization for the COVID-19 outbreak in Lombardy, Italy: early experience and forecast during an emergency response. JAMA. 2020;323(16):1545-6.
7. Yang X, Yu Y, Xu J, Shu H, Liu H, Wu Y et al. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study. The Lancet Respiratory Med. 2020;8(5):475-81.
8. Spoletini G, Hill NS. High-flow nasal oxygen versus noninvasive ventilation for hypoxemic respiratory failure: Do we know enough?. Ann Thoracic Med. 2016;11(3):163.
9. Alhazzani W, Møller MH, Arabi YM, Loeb M, Gong MN, Fan E et al. Surviving Sepsis Campaign: guidelines on the management of critically ill adults with Coronavirus Disease 2019 (COVID-19). Intensive Care Med. 2020;46(5):854-87.
10. Roca O, Caralt B, Messika J, Samper M, Sztrymf B, Hernández G et al. An index combining respiratory rate and oxygenation to predict outcome of nasal high-flow therapy. Am J Res Critical Care Med. 2019;199(11):1368-76.
11. Rapp JL, Lieberman-Cribbin W, Tuminello S, Taioli E. Male sex, severe obesity, older age, and chronic kidney disease are associated with COVID-

19 severity and mortality in New York City. Chest. 2021;159(1):112-5.
12. Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus–infected pneumonia in Wuhan, China. JAMA. 2020;323(11):1061-9.
13. Alizadehsani R, Sani AZ, Behjati M, Roshanzamir Z, Hussain S, Abedini N et al. Risk factors prediction, clinical outcomes, and mortality in COVID-19 patients. J Med Virol. 2021;93(4):2307-20.
14. Festic E, Bansal V, Kor DJ, Gajic O. US Critical Illness and Injury Trials Group: Lung Injury Prevention Study Investigators (USCIITG–LIPS). SpO2/FiO2 ratio on hospital admission is an indicator of early acute respiratory distress syndrome development among patients at risk. J Intensive Care Med. 2015;30(4):209-16.
15. Gandhi RT, Lynch JB, Del Rio C. Mild or moderate Covid-19. New England Journal of Medicine. 2020;383(18):1757-66.
16. Zucman N, Mullaert J, Roux D, Roca O, Ricard JD. Prediction of outcome of nasal high flow use during COVID-19-related acute hypoxemic respiratory failure. Intensive Care Med. 2020;46(10):1924-6.
17. Hasanin A, de Vasconcellos K, Abdulatif M. COVID-19 in Africa: current difficulties and future challenges considering the ACCCOS study. Anaesthesia, Critical Care Pain Med. 2021;40(4):24-8.
18. Mukhtar A, Lotfy A, Hasanin A, El-Hefnawy I, El Adawy A. Outcome of non-invasive ventilation in COVID-19 critically ill patients: a retrospective observational study. Anaesthesia, Critical Care Pain Med. 2020;39(5):579.
19. Mahdjoub E, Mohammad W, Lefevre T, Debray MP, Khalil A. Admission chest CT score predicts 5-day outcome in patients with COVID-19. Intensive Care Med. 2020;46(8):1648-50.

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