How to Cite:
Alessa, A., Allehyani, B., Bsooki, M., Ismail, M., Almaqati, S., Alkarmy, S., Alemam, S., Qatirgi, H., Mohorjy, D., & Alshaikhi, Z. (2022). The impact of calculating ROX index in delaying intubation with COVID-19 patients at King Abdullah medical city. *International Journal of Health Sciences*, *6*(S6), 10156–10165.
https://doi.org/10.53730/ijhs.v6nS6.12644

The impact of calculating ROX index in delaying intubation with COVID-19 patients at King Abdullah medical city

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International Journal of Health Sciences ISSN 2550-6978 E-ISSN 2550-696X © 2022.
Manuscript submitted: 9 May 2022, Manuscript revised: 18 July 2022, Accepted for publication: 27 August 2022

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Abstract---Background: HFNC is a respiratory mask that covers the nose like an oxygen mask, with the addition of nasal prongs to deliver extra oxygen. At 12 hours, a ROX score above or equal to 4.88 predicts a decreased probability of progressing to mechanical ventilation. Objective: The aim of this study was to evaluate using a high-flow nasal cannula as a potential predictor of delaying intubation. In doing this, the study also sought to verify whether the ROX index accurately predicts HFNC failure for COVID-19 patients treated in the intensive care unit (ICU). Method: Using retrospective observational analysis of prospectively collected data and the study population of patients in the ICUs at KAMC, the study collects and analyzes data using SPSS. Results: P values that are < 0.05 show that the mean differences are statistically significant, and this is seen on days 1-1, day 1-2, day2-1, day 2-2, day 3-1, day 3-2, day 4-2, day 10-1, and day 10-2. This suggests that ROX index can be used in intubation prediction with COVID-19 patients who have respiratory failure type I that received HFNC therapy. Conclusion: The study establishes that ROX index is a suitable parameter in intubation prediction in patients with Covid-19 that received HFNC therapy. It can be inferred from the analysis that the ROX index's higher value is linked with a higher chance of the success of the HFNC therapy and, consequently, a lower risk of mortality. ROX index at days 10-2, with a cut-off point of 5.35, predicts HFNC success in patients.

Keywords---acute respiratory failure, COVID-19, endotracheal intubation, high-flow nasal cannula, oxygen therapy, SARS-CoV-2, HFNC, Healthcare, ROX Index.

Background and Literature Review

High flow nasal cannula (HFNC) is an essential treatment for patients with ARF (acute respiratory failure), which is also a key symptom of Covid-19, and as Ferrer

et al. (2021) explains, the ROX index (Respiratory Organ Dysfunction Index) is used to predict the success of HFNC in Covid 19 patients. ROX is described as the ratio of FIO2 and SpO2 to respiratory rate (Cornillon et al., 2021; Cysneiros et al., 2020). HFNC is a respiratory mask that covers the nose like an oxygen mask, with the addition of nasal prongs to deliver extra oxygen. At 12 hours, a ROX score above or equal to 4.88 predicts a decreased probability of progressing to mechanical ventilation (Cysneiros et al., 2020). Healthcare organizations can use the scale on emergency intubation patients to help hospitals and physicians determine if a patient should be intubated or cancel intubation attempts. Emergency physicians developed this tool at King Abdullah University Hospital (KAUH) to help make these decisions when dealing with cardiac arrest patients (Ferrer et al., 2021). While it is hard to know precisely how many lives have been saved because of ROX score calculations, it is reasonable to assume that many more people are being helped daily. The figure below shows the measurement of ROX index.

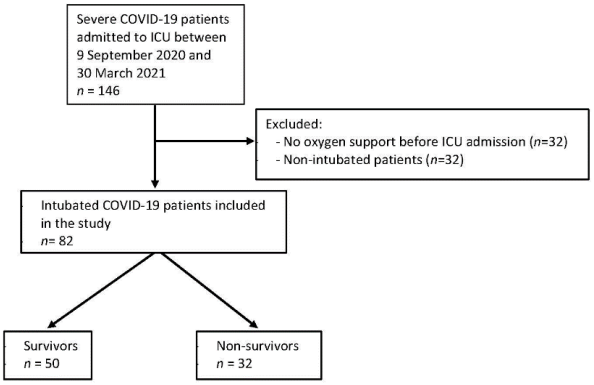

Figure 1. source Leszek et al (2021)

The index can be calculated for an individual patient and per population. Interpretation of these values needs to consider clinical factors (Liu et al., 2020; Roca et al., 2016). According to Ghani et al. (2021), a positive value indicates poor survival. A negative value can reflect either small sample size or a better outcome than expected, such as when physicians are often reluctant to intubate, leading to longer times on high-flow oxygen with better outcomes than people would predict based on historical controls. However, Vega et al. (2022) believe that negative values have no clear interpretation. They could represent poorer than expected results, but they could also mean that interventions, such as mechanical ventilation, are being performed to improve overall survival. The true impact of any intervention will always depend on how well patients did who were not treated with that intervention.

Intubation delay has been associated with higher morbidity and death. Several clinical factors such as the severity of illness, demographic factors, and others have been correlated with intubation delays. Even outside the intensive care unit (ICU), the HFNC is used to treat acute hypoxemic respiratory failure (AHRF), and the ROX index may be used to predict HFNC failure (Vega et al., 2022; Junhai et al., 2021; Suliman et al., 2021; Nguyen et al., 2021). The fundamental purpose of this research is to assess the ROX index using a high-flow nasal cannula as a

potential predictor of delaying intubation. Moreover, the study will verify whether the ROX index accurately predicts HFNC failure for COVID-19 patients treated inside the ICU. The figure below shows the management of critically ill patients with Covid-19 in the intensive care unit;

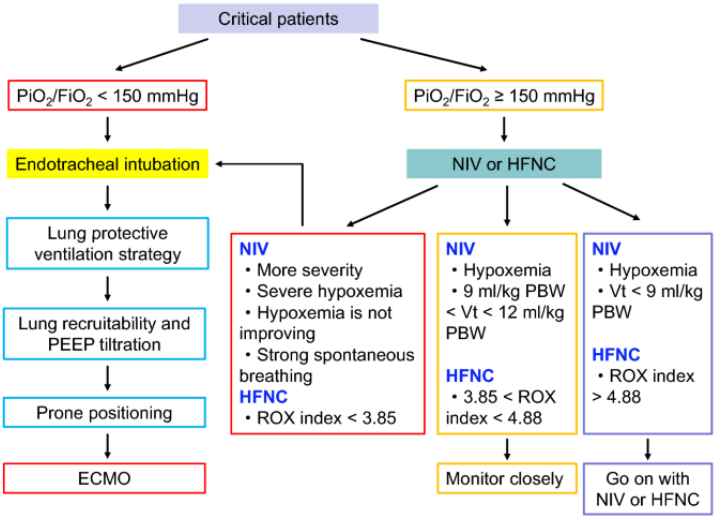

Figure 2. Management of Covid 19 patients, source Shang et al (2020)

As optimal timing of the Covid-19 mechanical ventilation is uncertain, Chandel et al. (2021) investigated the results of delayed intubation and assessed the ROX in predicting weaning from HFNC in COVID-19 patients. Findings proved HFNC a viable parameter. However, mechanical ventilation was an unnecessary strategy in numerous patients. For a majority that continued with mechanical ventilation, the period of using HFNC failed to separate patients with worse clinical results. The index was declared sensitive for identifying patients successfully weaned from HFNC. Ferrer et al. (2021) aimed to determine whether the ROX index would effectively predict the success of HFNC for patients that had contacted SARS-CoV-2 pneumonia. From the study, the researcher discovered that the ROX index at 24 h with a 5.35 cut-off point predicted the success of the therapy in SARS-CoV-2-induced ARF patients.

Dawning et al. (2021) conducted a multicenter retrospective study of adults admitted for suspected or known Covid-19 cases and treated with awake PP in the emergency department. It is essential to understand that the primary result was common in intubation during the beginning of hospitalization. Other results were from intubated patients within 48 hours of mortality and admission. Findings from the researchers showed that among the patients undergoing awake PP treatment in the emergency department before admission, the P/F ratio and ROX index, particularly following 24 hours after their admission, could be a valuable tool in establishing patients with a higher risk of intubation. Claudi et al. 2022 conducted a systematic review using online databases to acquire eligible articles whose data was published from preprints and observational studies. Data collected showed that the ROX was a suitable parameter in intubation prediction in patients that tested positive for Covid-19 that received HFNC therapy. Most

importantly, the ROX index's higher value was linked with a higher chance of the success of the HFNC therapy and, consequently, a lower risk of mortality.

Ceylan et al. (2022) aimed to verify the effectiveness of mROX and ROX in predicting the need for intubation in patients undergoing HFNO therapy in the ICU. Results showed that the overall mortality rate in patients showing similar laboratory and demographic data was 60,97%. The mROX and ROX cut-off values for intubation prediction at 6 hours were determined as 6,01 and 4,95. With that data, the researcher concluded that the indices could predict the invasive ventilation need for Covid-19 follow-up patients under the HFNO therapy. Additionally, data could aid in preventing adverse results. Delayed mechanical ventilation and intubation are closely linked with poor results. Therefore, Karim et al. (2022) assessed the association and utility between mROX and ROX indices in patients testing positive for Covid-19 that had started HFNC. Findings showed that both the indices, at 6h and baseline, presented a fair-to-good sensitivity, specificity, and negative and positive predictive values. In the ROC area, the difference showed statistical insignificance. The accuracy of both indices increased at the six-hour mark than from the baseline. Despite both indices' efficiency, only a 4.05 mROX at 6h presented sensitivity plus a 156% specificity that could be a clinically valuable screener. As the intubation timing in the Covid-19 period is controversial, Vest et al. (2022) wanted to identify the link between the ROX index, explained as the saturation of oxygen divided by the oxygen-inspired fraction divided by the frequency of breathing at the intubation time with clinical results. Focusing on intubated patients testing positive for the Coronavirus disease, results showed that a higher ROX at the intubation time had a positive association with survival among the ultimately intubated patients.

Aim and Objectives

This study aims to evaluate using a high-flow nasal cannula as a potential predictor of delaying intubation. The study also sought to achieve the following objective:

- To verify whether the ROX index accurately predicts HFNC failure for COVID-19 patients treated in the intensive care unit (ICU).

Methodology

The study design was a retrospective observational analysis of prospectively collected data, and the study population constituted patients in the ICUs at KAMC from 1 February 2020 until 30 December 2021. The inclusion criteria in this study was as follows:

- Male and female ≥18 years
- Patients presenting to KAMC with positive COVID-19 test
- Attending ICUs and required a high flow nasal cannula management

The exclusion criteria was as follows:

- Patients <18 years

- Patients presenting to KAMC with negative COVID-19 test
- Not required a high flow nasal cannula management
- Pregnant women

The sample size in this study was 136 patients who had COVID-19 and needed HFNC.

Outcome Assessment

- Time of applying high flow nasal cannula until either eliminate it or intubate the patient
- Calculate the ROX index every 12 hours and compare it with the ROX interpretation.

Example of how the ROX index can be used as a clinical tool to guide intubation decisions:

ROX index	
≥ 4.88	Little risk of intubation
3.85 – 4.87	Monitor due to increased risk of intubation
2.85 – 3.84	Close monitoring in ICU if possible. High risk of needing intubation
< 2.85	Consider intubation

Discussion

The analysis uses both descriptive and inferential statistics and using SPSS. The researcher can determine whether the ROX index accurately predicts HFNC failure for COVID-19 patients treated in the intensive care unit (ICU). As shown in the table below, the sample size in this study was 136, with 46.3% of these intubated and 53.7% weaned off. A relatively large standard deviation of 2.83 with a mean of 3.51 indicates that the responses varied greatly.

Table 1
Demographic and Clinical Data of the Study Population

ROX	N= 136 (%)	Mean ± SD
Day of HFNC use	136 (100)	3.51 ± 2.83
Result Intubated Weaned off	 63 (46.3) 73 (53.7)	 -

Note SD: standard deviation, N: number of responses.

Table 2 below shows the ROX index on different days. The highest mean ROX index between day 1 and day 15 was 8.22, and the lowest ROX index was 4.88. The standard deviations are relatively large relative to the mean, indicating that the ROX index also varied significantly over the experiment period.

Table 2
ROX index

ROX	N= 136 (%)	Mean ± SD
day 1-1	136 (100)	6.04 ± 2.70
day 1-2	133 (97.8)	6.86 ± 2.87
day 2-1	108 (79.4)	6.80 ± 2.63
day 2-2	90 (66.2)	7.21 ± 3.35
day 3-1	71 (52.2)	6.40 ± 2.43
day 3-2	61 (44.9)	6.79 ± 3.09
day 4-1	57 (41.9)	6.82 ± 2.97
day 4-2	48 (35.3)	6.50 ± 2.74
day 5-1	43 (31.6)	6.83 ± 3.01
day 5-2	38 (27.9)	7.19 ± 2.52
day 6-1	31 (22.8)	7.63 ± 2.76
day 6-2	25 (18.4)	7.36 ± 2.75
day 7-1	19 (14)	8.02 ± 3.55
day 7-2	16 (11.8)	6.87 ± 2.49
day 8-2	13 (9.6)	6.87 ± 2.48
day 8-1	11 (8.1)	6.77 ± 2.97
day 9-1	10 (7.4)	6.78 ± 4.16
day 9-2	9 (6.6)	6.96 ± 3.91
day 10-1	7 (94.9)	7.08 ± 3.11
day 10-2	7 (5.1)	5.82 ± 1.60
day 11-1	5 (3.7)	8.22 ± 3.34
day 11-2	4 (2.9)	7.60 ± 2.97
day 12-1	4 (2.9)	8.20 ± 3.69
day 12-2	3 (2.2)	7.38 ± 3.34
day 13-1	2 (1.5)	4.88 ± 2.79
day 13-2	1 (.7)	6.64
day 14-1	1 (.7)	28
day 14-2	0	-
day 15-1	0	-
day 15-2	0	-

Note SD: standard deviation, N: number of responses.

The t-test statistics in the table below show whether or not the mean differences between intubated and weaned off. Intubation refers to helping a patient with difficulty breathing and weaning off, relieving a patient from mechanical breathing support. In table 3 below, the p values that are < 0.05 show that the mean differences are statistically significant, and this is seen on days 1-1, day 1-2, day2-1, day 2-2, day 3-1, day 3-2, day 4-2, day 10-1, and day 10-2. This implies that ROX can be used in intubation prediction in patients with respiratory problems that received HFNC therapy. From the mean differences, it can be concluded that the ROX index's higher value can be associated with a higher chance of the success of the HFNC therapy.

Table 3
The results of the T-Test regarding Intubated and Weaned off

Scale	t	DF	p-value	Mean Diff.	Standard Error of Diff.	95% Confidence Interval for Diff.	
						Lower	Upper
day 1-1	-3.26	130	.001*	-1.43	.43	-2.30	-.56
day 1-2	-4.96	124.5	.000*	-2.22	.44	-3.11	-1.33
day 2-1	-3.32	106	.001*	-1.62	.48	-2.58	-.65
day 2-2	-4.90	88	.000*	-3.12	.63	-4.39	-1.85
day 3-1	-2.58	69	.012*	-1.44	.55	-2.55	-.33
day 3-2	-2.40	59	.019*	-1.86	.77	-3.41	-.31
day 4-1	-1.61	55	.112	-1.27	.79	-2.86	.30
day 4-2	-2.41	46	.020*	-1.84	.76	-3.38	-.30
day 5-1	-1.96	41	.056	-1.76	.90	-3.59	.05
day 5-2	-1.99	36	.054	-1.58	.79	-3.20	.03
day 6-1	-1.70	29	.100	-1.68	.99	-3.70	.34
day 6-2	-1.93	23	.066	-2.06	1.06	-4.27	.14
day 7-1	-1.96	20	.064	-2.06	1.05	-4.25	.12
day 7-2	-1.16	17	.260	-1.90	1.63	-5.35	1.54
day 8-2	-1.78	14	.096	-2.09	1.17	-4.60	.41
day 8-1	-1.57	8.7	.150	-1.96	1.24	-4.79	.86
day 9-1	-1.70	9	.123	-2.81	1.65	-6.55	.92
day 9-2	-2.19	8	.059	-4.84	2.20	-9.92	.23
day 10-1	-3.20	7	.015*	-5.73	1.78	-9.96	-1.49
day 10-2	-6.23	5	.002*	-5.48	.88	-7.75	-3.22
day 11-1	-1.34	5	.237	-1.55	1.15	-4.51	1.41
day 11-2	-2.52	3	.086	-5.02	1.99	-11.36	1.31
day 12-1	.04	2	.969	.18	4.20	-17.89	18.26
day 12-2	-1.10	2	.386	-4.54	4.12	-22.29	13.20

Note: Significant at $p < 0.05$ level

Conclusion

The analysis presents sufficient evidence to conclude that ROX is a suitable parameter in intubation prediction in patients with Covid-19 that received HFNC therapy. It can be inferred from the analysis that the ROX index's higher value is linked with a higher chance of the success of the HFNC therapy and, consequently, a lower risk of mortality. ROX index at days 10-2, with a cut-off point of 5.35, predicts HFNC success in patients.

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