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Original Article

Early Prediction of High-Flow Nasal Cannula Success or Failure using ROX and Modified ROX Index Incorporating Heart Rate in Patients with Acute Hypoxemic Respiratory Failure

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Abstract

Background and Aim: The use of high-flow nasal cannula (HFNC) in acute hypoxic respiratory failure decreases intubation rates and lowers mortality. However, early prediction of HFNC failure is very important, as it may delay the much-needed intubation. To address this issue, ROX index and ROX-HR index were calculated and compared.

Methods: Thirty patients of either sex in the age group of 18–60 years of ASA grade I & II presenting with acute hypoxemic respiratory failure were put on HFNC after taking informed consent. Baseline hemodynamic parameters, APACHE II, Q SOFA score and Charleson Comorbidity Index, and ABG were noted, and continuous monitoring of the above parameters was done. ROX index and ROX-HR index were calculated at specified intervals in patients of HFNC success and failure and were compared for their sensitivity, specificity, positive predictive value, and negative predictive value in predicting HFNC success or failure.

Results: Twenty-one patients were weaned from HFNC and 9 patients were shifted to a higher mode of oxygenation. There was no positive correlation of age with HFNC success and failure. In HFNC success, heart rate (HR) and respiratory rate (RR) improved over time and patients were weaned off. In HFNC failure, HR and RR both had increasing trends and needed vasopressors to maintain blood pressure. ROX and ROX-HR index values improved (>5.90 and >6.90, respectively) at 6 h in HFNC success patients. At 8 h, both indices were equally sensitive. At 6 h, the specificity of ROX-HR was more.

Conclusion: ROX index and ROX-HR index are sensitive in the early prediction of HFNC success. ROX-HR index is more specific for the prediction of HFNC failure.

Key words: High-flow nasal cannula, Acute respiratory failure, ROX index, ROX-HR index

INTRODUCTION

High-flow nasal cannula (HFNC) therapy has been gaining attention in the management of acute hypoxemic respiratory failure as it delivers heated and humidified oxygen at flow rates of up to 60 L/min, a PEEP of 3–5 cm H_2O, with the maintenance of constant fraction of inspired oxygen. It reduces anatomical dead space and provides positive end-expiratory pressure,[1,2] thereby decreasing respiratory rate (RR) and improving oxygenation.[3] The use of HFNC in patients of acute hypoxemic respiratory failure[4] decreases the intubation rates and lowers mortality. However, delayed detection of HFNC failure carries the risk of delaying much-needed intubation. To address this problem, various parameters were used for early prediction of HFNC success or failure. ROX index, defined as the

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ratio of oxygen saturation as measured by pulse oximetry to the fraction of inspired oxygen (SpO_2/FiO_2) to RR, has been used to predict HFNC success and failure.[5] As heart rate is the most commonly measured parameter in the intensive care unit patients and by incorporating it in the ROX index may improve its diagnostic accuracy for prediction of HFNC success and failure. ROX-HR index defined as the ratio of ROX index over heart rate (beats/min) multiplied by factor 100 was formulated. Heart rate has an inverse ratio to HFNC success as tachycardia as early as 1 h into HFNC therapy is found to be associated with HFNC failure. As nowadays, HFNC is being commonly used in patients of acute hypoxic respiratory failure to delay unwanted intubations.[6] It is necessary to formulate certain parameters to monitor the progress of HFNC therapy so that delayed intubations can be avoided. Hence, the present study was designed with the primary aim of evaluating the efficacy of the ROX index and ROX-HR index in early prediction of HFNC success and failure by comparing their sensitivity i.e., the percentage of correctly predicted HFNC success as a proportion of all successful HFNC trial, specificity which is defined as the percentage of correctly predicted HFNC failures as a proportion of all failed HFNC trials, positive predictive value (PPV) i.e., the percentage of all correctly predicted successful HFNC trials as a proportion of all predicted successful HFNC trials and negative predictive value (NPV) i.e., the percentage of correctly predicted failed HFNC trials as a proportion of all predicted failed HFNC trials. Secondary aim was to note the duration of HFNC therapy and the number of patients with HFNC success and failure.[7]

MATERIALS AND METHODS

This prospective observational study was conducted on 30 patients aged 18–60 years of ASA grades I and II presenting with acute respiratory failure after taking informed consent and approval from the institutional ethics committee (3371/D-26/2020 batch).

Patients with acute hypoxemic respiratory failure with a RR >25 breaths/min and a P/F ratio of <300 mmHg on an oxygen device delivering ≥10 L/min of oxygen were included in the study. Patients having chronic respiratory failure, hypercapnia ($PaCO_2$ >45 mmHg), acute respiratory failure secondary to asthma, chronic obstructive pulmonary disease exacerbation, hemodynamic instability requiring vasopressor support, Glasgow Coma Scale (GCS) <12, epistaxis, and recent facial or nasal surgery were excluded from the study. Baseline investigations such as complete blood count, liver function tests, renal function tests, electrolytes, ABG, coagulation profile, chest X-ray, and ECG were done. Baseline heart rate, RR, NIBP, ECG, SpO_2, ABG, GCS score, APACHE II score, q SOFA score, mode of oxygen therapy and FiO_2, and Charleson Comorbidity Index (CCI) were noted before the start of HFNC therapy.

Patients were attached to HFNC and initiated at a minimum flow of 40L/min which was increased to 60L/min and FiO_2 was adjusted to maintain a target SpO_2 of greater than or equal to 92%. After putting on HFNC, patients were monitored for heart rate, non-invasive blood pressure, RR, SpO_2, ECG, temperature, and ABG at regular intervals. General well-being of the patients was assessed using APACE II, q SOFA score, and CCI on a daily basis. Laboratory investigations were done depending on the condition of the patient. During HFNC therapy, the ROX index and ROX-HR index were calculated at regular intervals by continuous monitoring of RR, HR, SpO_2, and FiO_2 given. Both were recorded before the initiation of HFNC therapy, and then, after 1 h, 2 h, 4 h, 6 h, 8 h, 10 h, 12 h, 18 h, 24 h, and 48 h; once daily till HFNC therapy continued and 1 h before termination of HFNC.

Oxygenation with HFNC was continued till either HFNC success, i.e., maintaining SpO_2 >92% with FiO_2 <60% independent of gas flow or HFNC failure, i.e., worsening respiratory condition or at least two of the following criteria: failure to achieve correct oxygenation (PaO_2 <60 mmHg or SpO_2 <90% despite HFNC flow >30 L/min and FiO_2 of 1), respiratory acidosis ($PaCO_2$ >50 mmHg with pH <7.25), RR >30 breaths/min or inability to clear secretions, and patients were shifted to NIV or invasive ventilation. The total duration of HFNC therapy in days was calculated, and patients weaned or failure from HFNC therapy were noted. Sensitivity, specificity, NPV and PPV of ROX index, and ROX-HR index were calculated.

Statistical Analysis

Required sample size was calculated using an a priori sample size calculator. Input: Tails: 1, slope H1 = 0.15, α error probability = 0.05, power = 0.95, standard deviation σ-x = 1.9, standard deviation σ-y =0.5. Output: No centrality parameter = 3.3985716, critical t = 1.7171444, and Df = 22. Total sample size = 24.

The data from the present study were systematically collected, compiled, and statistically analyzed using the software IBM SPSS 22.0 to draw relevant conclusions. Data were expressed as means, standard deviation, numbers, and percentages. The intragroup comparison of the parametric data was done using the "*t*" test. The "*P*"-value was determined to finally evaluate the levels of significance. $P < 0.05$ was considered significant, and a $P < 0.001$ was considered highly significant. Power analysis was done to calculate the power of the study. It was 95% by taking α error 0.05.

RESULTS

In the present study, 30 patients were put on HFNC therapy. Twenty-one patients were successfully weaned off (HFNC success) and nine patients needed NIV support or mechanical ventilation (considered HFNC failure). The demographic profile, baseline hemodynamic parameters, APACHE II, q SOFA score, and CCI were recorded in patients with HFNC success and failure, as shown in Table 1.

After putting patients on HFNC, continuous monitoring of heart rate was done. Difference in the mean HR in HFNC success and failure was statistically non-significant ($P > 0.05$) till 6 h. From 8 h onwards, mean HR started increasing in failure patients and was stable in patients who were successfully weaned off ($P < 0.05$), as shown in Graph 1. RR was high in HFNC failure patients as compared to HFNC success patients but the difference was non-significant ($P > 0.05$) from initiation of HFNC till 6 h. The value of RR started worsening in failure patients at 8 h and was normal in HFNC success patients ($P < 0.05$) till the patients were weaned off or shifted to a higher mode of oxygenation, as shown in Figure 1. Systolic and diastolic blood pressure was monitored at regular intervals, patients who failed HFNC therapy had fall in BP from 6 h onward and needed vasopressor support. SBP and DBP from 10 h onwards were significantly low in HFNC failure patients ($P < 0.05$), as shown in Figure 2. Patients who failed HFNC therapy, baseline APACHE II score, and q SOFA score were high (18.44 ± 4.22 and1.89 ± 0.93, respectively) as compared to HFNC success (12.56 ± 1.33 and 1.11 ± 0.33, respectively), and remained on the higher side till the patients were shifted to NIV of MV ($P < 0.05$). However, CCI at the initiation of therapy and throughout therapy was statistically comparable in HFNC success and failure patients. At the initiation of HFNC till 8 h, FiO_2 requirement in patients with HFNC success was lower (84.71 ± 6.99) as compared to HFNC failure (93.89 ± 7.04) but the difference was not significant $P > 0.05$. From 10 h onward, FiO_2 requirement decreased in patients who were successfully weaned but in HFNC failure patients required significantly more FiO_2 to maintain $SpO_2 \geq 92\%$, $P < 0.05$), as shown in Table 2.

ROX index and ROX-HR index were calculated using RR, HR, SpO_2, and FiO_2 at various time intervals to predict HFNC success (ROX >5.90 and ROX HR >6.90) and failure (ROX <5.90 and ROX HR <6.90). Both ROX and ROX-HR index were comparable from initiation of HFNC till 4 h in HFNC success and failure patients ($P > 0.05$), but 6 h onward, both started increasing in success patients and were significantly low in failure patients $P < 0.05$, as shown in Table 3.

ROX and ROX-HR indexes were compared for their ability to early predict HFNC success or failure by comparing their sensitivity, specificity, PPV, and NPV, as shown in

Table 1: Comparing baseline demographic, hemodynamic characteristics in patients with acute hypoxemic respiratory failure

Baseline parameters	HFNC success (n=21)	HFNC failure (n=9)	P value
Age (years)	43 (41-50)	41 (39-50)	0.193
Male	11 (36.67)	5 (16.67)	0.871
Female	10 (33.33)	4 (13.33)	0.871
APACHE II score	12.56±1.33	18.44±4.2	0.00
q SOFA	1.11±0.3	1.89±0.93	0.02
CCI	1.44±1.34	1.11±1.05	0.27
Heart rate (beats/min)	93±5.07	96±4.64	0.15
Respiratory rate (breaths/min)	21.62.0±4	22.8±4.31	0.41
SBP (mmHg)	123.81±9.28	130.22±8.17	0.08
DBP (mmHg)	76.29±5.81	78.78±6.89	0.16
SpO_2	90.00±2.50	90.33±4.12	0.500

*SBP (systolic blood pressure), DBP (diastolic blood pressure), SpO_2 (oxygen saturation)
*S– Significant (p<0.05), NS- Non significant (p>0.05)

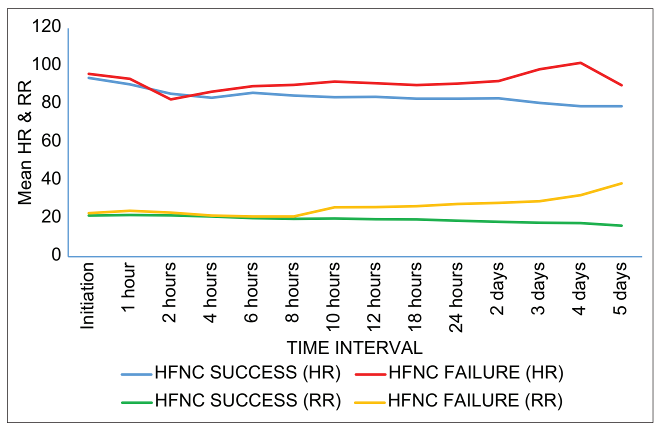

Figure 1: Depicting changes in mean HR and RR in patients with high-flow nasal cannula success and failure at various time intervals

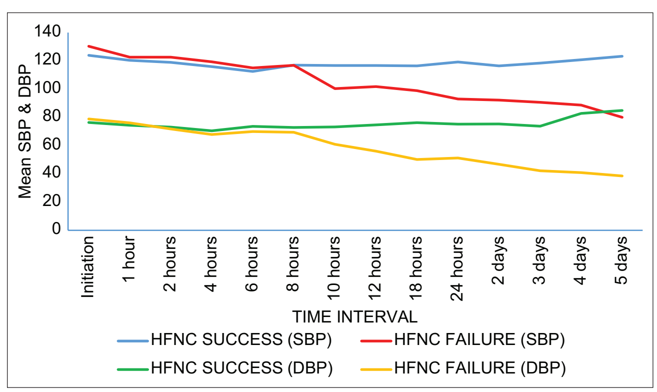

Figure 2: Depicting changes in mean systolic blood pressure and mean diastolic blood pressure at various time intervals in patients with high-flow nasal cannula success and failure

Table 4. It was observed that at 2 h, the sensitivity and specificity of ROX and ROX-HR were comparable, started increasing at 4 h, but remained comparable. At 6 h, the sensitivity of both indexes was still comparable but the specificity of ROX-HR increased (77.785%). At 8 h, the sensitivity of both indexes was again comparable but the specificity of the ROX-HR index (77.78%) was more than the ROX index (55.56%). At 10 and 12 h, the sensitivity remained comparable but the specificity was more of the ROX-HR index and thereafter the specificity of ROX-HR remained high. The mean duration of HFNC therapy in patients who were successfully weaned was 2.851 ± 1.118 days and in HFNC failure patients was 3.666 ± 1.118 days ($P = 0.205$).

Table 2: FiO_2 changes in patients with HFNC success and failure

	Hfnc success (n=21)	Hfnc failure (N=9)	P-value
FIO2	**Mean±SD**	**Mean±SD**	**p-value**
Initiation	84.71±6.99	93.89±7.04	0.500
1 hour	82.38±8.97	89.89±6.94	0.260
2 hours	78.81±10.33	87.56±6.71	0.170
4 hours	76.10±9.49	83.67±6.20	0.090
6 hours	72.48±10.78	80.56±7.68	0.140
8 hours	69.24±10.65	78.67±8.65	0.320
10 hours	64.67±12.08	78.44±8.63	0.030
12 hours	61.10±12.29	82.33±7.52	0.010
18 hours	55.43±12.81	80.00±7.23	0.000
24 hours	51.24±15.39	78.11±7.96	0.000
2 days	45.83±17.35	74.56±7.95	0.000
3 days	40.77±13.67	72.57±9.29	0.000
4 days	40.00±13.23	69.17±8.01	0.000
5 days	36.67±11.69	77.50±3.54	0.000

*S– Significant (p<0.05), NS- Non significant (p>0.05)

DISCUSSION

In the present study, 30 patients were put on HFNC therapy, out of which 21 patients were successfully weaned off from HFNC and 9 patients failed HFNC therapy and required a higher mode of oxygenation either NIV or ventilator support. In the present study, 18–60 years age group patients were included. It was observed that the age of the patient had no positive correlation with HFNC success or failure. Out of 30 patients, 14 were females and 16 were males. Among 14 females, 10 were successfully weaned and among 16 males, 11 were successfully weaned. Hence, the sex of patients had no significant effect on HFNC success and failure. Alshahrani *et al*.[8] and Kerai *et al*.[9] also observed that the age of the patient and sex of the patient have no significant effect on HFNC success and failure.

In the present study, baseline APACHE II score and q SOFA score were high in patients who failed on HFNC therapy (13.44 ± 4.22 and 1.89 ± 0.93, respectively) as compared to patients who were successfully weaned (12.59 ± 1.33 and 1.11 ± 0.33, respectively) and both scores significantly improved over the time in HFNC success patients. Previous studies also observed that patients who had high APACHE II and q SOFA scores before initiation of HFNC therapy needed a higher mode of oxygenation as compared to patients who had lower scores.[7,9,1011] Charlson Comorbidity Index (CCI) was used to assess the comorbidities in patients before initiation on HFNC therapy and on subsequent days of therapy. CCI was comparable at all measured intervals in HFNC success and failure patients. Goh *et al*.[11] assessed CCI before initiation of HFNC therapy and observed that values of CCI were comparable in patients of HFNC success and

Table 3: ROX INDEX and ROX-HR INDEX trend at various time intervals in patients with HFNC success and failure

Time interval	ROX Index			ROX- HR		
	Patients with HFNC success (n=21)	Patients with HFNC failure (n=9)	p-value	Patients with HFNC success (n=21)	Patients with HFNC failure (n=9)	p-value
	Mean±SD	**Mean±SD**		**Mean±SD**	**Mean±SD**	
Initiation	5.32±0.51	5.10±1.05	0.418	5.18±0.59	4.89±1.19	0.375
1 hour	5.39±0.79	5.18±0.60	0.385	5.46±0.90	4.91±0.69	0.101
2 hours	5.67±0.65	4.80±0.52	0.080	6.17±0.72	5.87±0.81	0.320
4 hours	6.05±0.87	5.81±0.57	0.455	7.23±1.15	6.86±0.92	0.401
6 hours	6.72±1.38	5.61±0.52	0.010	8.06±1.73	6.26±0.49	0.000
8 hours	7.11±1.28	5.81±0.76	0.000	8.62±1.63	6.19±0.58	0.000
10 hours	7.72±1.55	5.81±0.57	0.000	9.15±2.21	6.34±0.60	0.000
12 hours	8.34±1.81	5.44±0.66	0.000	9.99±2.39	5.96±0.57	0.000
18 hours	9.32±2.14	5.66±0.78	0.000	11.06±3.09	6.29±0.67	0.000
24 hours	10.92±3.50	5.68±0.87	0.000	13.25±4.44	6.22±0.45	0.000
2 days	12.74±4.27	5.77±1.18	0.000	15.41±5.30	6.25±0.67	0.000
3 days	14.30±6.68	5.76±1.47	0.000	17.70±8.02	5.80±0.72	0.000
4 days	13.90±3.67	6.13±1.99	0.000	17.72±5.03	5.93±1.06	0.000
5 days	14.35±1.85	5.00±0.47	0.000	18.26±2.88	5.56±0.52	0.000

*S– Significant (p<0.05), NS- Non significant (p>0.05)

Table 4: Comparison of ROX and ROX HR index in terms of sensitivity, specificity, PPV, NPV

ROX and ROX-HR index at time intervals	N	Sensitivity(%)	Specificity(%)	PPV(%)	NPV(%)
2 hour ROX-HR>6.90	30	57.14	77.78	85.71	43.75
2 hour ROX>5.90	30	47.62	66.67	76.92	35.29
4 hour ROX-HR>6.90	30	61.90	66.67	81.25	42.86
4 hour ROX>5.90	30	52.38	66.67	78.57	37.50
6 hour ROX-HR>6.90	30	66.67	77.78	87.50	50.00
6 hour ROX>5.90	30	61.90	55.56	76.47	38.46
8 hour ROX-HR>6.90	30	71.43	77.78	88.24	53.85
8 hour ROX>5.90	30	71.43	55.56	78.95	43.45
10 hour ROX-HR>6.90	30	76.19	66.67	84.21	54.55
10 hour ROX>5.90	30	76.19	55.56	80.00	50.00
12 hour ROX-HR>6.90	30	76.19	66.67	84.21	54.55
12 hour ROX>5.90	30	80.95	44.44	77.27	50.00
18 hour ROX-HR>6.90	30	80.95	77.78	89.47	63.64
18 hour ROX>5.90	30	80.91	44.44	77.27	50.00
24 hour ROX-HR>6.90	30	85.71	88.89	94.74	72.73
24 hour ROX>5.90	30	85.71	44.44	78.26	57.14
Day 2 ROX-HR>6.90	24	80.00	88.89	92.31	72.73
Day 2 ROX>5.90	24	73.33	55.56	73.33	55.56
Day 3 ROX-HR>6.90	17	80.00	85.71	88.89	75.00
Day 3 ROX>5.90	17	80.00	57.14	72.73	66.67
Day 4 ROX-HR>6.90	14	87.50	83.33	87.50	83.33
Day 4 ROX>5.90	14	75.00	66.67	75.00	66.67
Day 5 ROX-HR>6.90	06	75.00	50.00	75.00	50.00
Day 5 ROX>5.90	06	75.00	50.00	75.00	50.00

*S– Significant (p<0.05), NS- Non significant (p>0.05)

failure. However Kim *et al.*[12] observed that in older age group patients, higher CCI is associated with HFNC failure.

In the present study, mean HR at the initiation of HFNC was comparable in patients with HFNC success (93.95 ± 5.07) and HFNC failure (96.00 ± 4.64). In HFNC success patients, the mean heart rate improved from 90.57 beats/min at 1 h to 84.62 beats/min at 8 h to 79 beats/min, when patients were weaned. However, in patients who failed HFNC therapy showed a worsening trend of HR from 88 beats/min at 1 h to 90.22 beats/min at 8 h to 112 beats/min when patients were shifted to a higher mode of oxygenation. Previous studies were done by Goh *et al.*,[11] ,Cho *et al.*,[13] Calligaro *et al.*,[14] and Lun *et al.*[16] in patients of acute hypoxemic respiratory failure who were put on HFNC observed that patients who had stable baseline HR and showed an improving trend of HR on subsequent intervals of HFNC therapy responded well and were successfully weaned from HFNC as compared to patients who showed an increasing trend in HR. Mean systolic blood pressure, diastolic blood pressure, and mean arterial pressure at the initiation of HFNC therapy were comparable in patients with HFNC success and failure. However, in patients who failed HFNC therapy, BP started decreasing from 10 h onward and needed more vasopressor support to maintain blood pressure. Kim *et al.*[12] and Cho *et al.*[13] and observed that patients who failed on HFNC therapy needed vasopressor support to maintain BP more frequently as compared to patients who were successfully weaned. In the present study, the mean RR before initiation of HFNC therapy was comparable in patients of HFNC success and failure. Mean RR started to decline from 21.62/min to 16.25/min in patients who were successfully weaned. However, in HFNC failure patients, there was an initial decline but after 8 h into therapy, RR increased till patients were shifted to a higher mode of oxygenation. Previous studies also observed that RR is a good predictor of HFNC success and failure as patients who were successfully weaned showed a decrease in RR after HFNC therapy as compared to patients who failed HFNC showed an increase in RR and needed a higher mode of oxygenation.[9,10-12,14]

In all 30 patients, HFNC was started at a flow rate of 40 L/min and gradually increased to 60 L/min if needed, and FiO_2 was adjusted to maintain $SPO_2 \geq 92\%$. It was observed that patients, who failed HFNC therapy, needed high flow rates and FiO_2 as compared to patients who were successfully weaned off, to maintain a target SpO_2 of 92%. Previous studies also supported these findings that patients who required high flow rates and FiO_2 to maintain desired saturation ultimately failed on HFNC, and needed a higher mode of oxygenation.[9,12-14]

ROX index and ROX-HR index were calculated. ROX index value <5.90 and ROX-HR index value <6.90 were taken as HFNC failure. ROX index was comparable at 1 h, 2 h, and 4 h in patients with HFNC success and failure patients. From 6 h onwards, the ROX index was >5.90 in patients who were successfully weaned, whereas in HFNC failure patients, the ROX index was <5.90 from 6 h onward till the patients were either intubated or put on NIV. Previous studies observed that HFNC success was associated with a greater increase in ROX index values.[9-11,14,15] Calligaro *et al*.[14] and Alshahrani *et al*.[8] observed that an improved ROX index value at 6 h is a good predictor of HFNC success. Kerai *et al*.[9] observed that the ROX index values at 2, 6, and 12 h of HFNC therapy were higher in HFNC success patients.

ROX-HR index was calculated using SpO_2, FiO_2, RR, and HR of patients at various time intervals. ROX-HR index remained comparable at initiation, 1 h, 2 h, and 4 h of HFNC therapy in all patients. From 6 h onward, ROX-HR index values remained on the higher side >6.90 in HFNC success and showed a declining trend of <6.90 in patients who failed HFNC therapy. Calligaro *et al*.[14] observed that the ROX-HR index performed better in HFNC success patients (3.44) and was low in HFNC failure patients (2.53). Goh *et al*.[11] observed that a ROX-HR index of >6.80 is associated with a lower risk of HFNC failure.

In the present study, it was observed that the sensitivity and specificity of ROX and ROX-HR index were comparable at 2 h and started increasing at 4 h. At 6 h sensitivity of both was comparable but the specificity of the ROX-HR index increased from 8 h onward and remained on the higher side. Therefore, the ROX-HR index is better in the early prediction of HFNC failure. Goh *et al*.[11] observed that the ROX-HR index was a better indicator in predicting early failure of HFNC therapy as its specificity was greater than the ROX index.

Limitations

It was a small sample size. The accuracy of the estimation process increases and the findings could be better extrapolated to the general population if the sample size was large. Another limitation was the age group of the study population which was 18–60 years. Hence, the ability of ROX and ROX-HR index for early prediction of HFNC success and failure in older age groups could not be evaluated.

CONCLUSION

ROX index and ROX-HR index, both are good in the early prediction of HFNC success, whereas the ROX-HR index is better in the early prediction of HFNC failure in patients of acute hypoxemic respiratory failure.

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