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An Index Combining Respiratory Rate and Oxygenation to Predict Outcome of Nasal High Flow Therapy.

Roca O[1,2], Caralt B[3], Messika J[4], Samper M[5], Sztrymf B[6], Hernández G[7], García-de-Acilu M[3], Frat JP[8] Masclans JR[10,5], Ricard JD[11].

Roca et al. 2018

American Journal of Respiratory and Critical Care Medicine

An Index Combining Respiratory Rate and Oxygenation to Predict Outcome of Nasal High Flow Therapy.

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Introducing the ROX Index

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2018

An index combining respiratory rate and oxygenation
to predict outcome of Nasal High Flow (NHF) therapy.

$$\frac{SpO_2}{FiO_2}$$
$$-RR$$

Roca et al. *Am J Respir Crit Care Med*. 2018 [Epub ahead of print].

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Key points

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- The ROX index can help to predict NHF therapy outcomes in patients with acute hypoxic respiratory failure (AHRF) due to pneumonia.
- The index can be calculated easily and repeatedly at the patient's bedside.
- The index is dynamic.

Roca et al. *Am J Respir Crit Care Med*. 2018 [Epub ahead of print].

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Background

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In a pilot study, Roca (2016) previously demonstrated that the ROX index:

- outperformed the diagnostic accuracy of its individual variables
- participants with an index ≥ 4.88 and > 12 hours of ongoing NHF therapy were less likely to be intubated, even after adjusting for potential covariates.

It was anticipated that the ratio of the ROX index may predict failure in adult AHRF patients on NHF therapy.

Further independent validation of this index was required.

Aim

- To validate the ROX index value of ≥ 4.88 as a determinant of NHF success at 2, 6, or 12 hours.
- To identify a series of ROX score margins for NHF failure at four time points.
- To perform external validations using the FLORALI study cohort (Frat, 2015).

Roca et al. *Am J Respir Crit Care Med*. 2018 [Epub ahead of print].

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Background

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Setting

Five French and Spanish ICUs 2016 - 2017

Population

N = 191, adults with AHRF* followed until death or discharge

**AHRF defined according to the IDSA / ATS 2007 guidelines.*

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Methods

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A multi-center prospective non-randomized observational cohort study.

INCLUSION CRITERIA	EXCLUSION CRITERIA
ICU patients with AHRF due to pneumonia, on NHF therapy	< 18 years old
	Indication for immediate intubation
	Limitation of therapy (DNR)
	Elective intubation for diagnostic or therapeutic procedures

Primary outcome

NHF failure* requiring invasive ventilation within study completion time.

**Failure defined by set of predetermined criteria for intubation.*

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Pre-determined criteria for intubation

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- GCS < 12
- Cardiac arrest
- Arrhythmias
- Severe hemodynamic instability
- Two or more of the following
  - PaO_2 < 60 mmHg or SpO_2 < 90% on NHF ≥ 30 L/min FiO_2 100%
  - Respiratory acidosis $PaCO_2$ > 50 mmHg or Pv CO_2 > 55 mmHg, pH < 7.25
  - RR > 30 BPM
  - Inability to clear secretions

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Methods

Treatment regimen

- Participants were on FM O_2 ≥ 10 L/min with SpO_2 < 92% and RR ≥ 25 breaths/min. NHF was initiated at 30 L/min, FiO_2 100%
- FiO_2 titrated with a target SpO_2 > 92%
- Flow rate adjusted according to the maximum tolerated rate – which was achieved within the first 10 mins of NHF treatment – for all participants.

Roca et al. *Am J Respir Crit Care Med*. 2018 [Epub ahead of print].

Methods

Outcome

- Accuracy of the ROX index for predicting NHF outcomes (need for intubation or not)
  - Determined through Cox proportional hazards modelling
  - ROX index was calculated as the ratio of SpO_2/ FiO_2 to RR
  - Variables with a positive association with NHF success were in the numerator field, and the variables with an inverse relation to NHF success were in the denominator field.

NHF failure definition

- Requiring intubation and invasive mechanical ventilation.

NHF success definition

- Not requiring intubation or invasive mechanical ventilation.

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Results

Baseline characteristics

CHARACTERISTIC	
Age (years)	63 (52 – 72)
Pneumonia severity index	116 (80 – 152)
APACHE II	16 (12 – 21)
SOFA ICU admission	5 (3 – 7)
Presence of shock (%)	20.4

At baseline these study participants were sicker than those enrolled in the pilot (Roca, 2016).

Results

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2018

ROX index threshold ≥ 4.88 (determinant for NHF success) was validated with three time points:

- 2 h (HR 0.434 [95% CI 0.264 – 0.715]; P= 0.001)
- 6 h (HR 0.304 [95% CI 0.182 – 0.509]; P<0.001)
- 12 h (HR 0.291 [95% CI 0.161 – 0.524]; P<0.001)

Three time points were validated for this threshold as opposed to one as previously described ≥ 12hrs (Roca, 2016).

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Results

Respiratory variables during NHF therapy comparing success vs. failure (median)

VARIABLE*	TIME	SUCCESS (N=123)	FAILURE (N=68)	P-VALUE#
SpO_2/FiO_2	Prior to NHF	180	106	0.005
	2 h	155	109	0.003
	6 h	160	115	0.001
	12 h	165	113	0.001
	18 h	176	118	0.002
	24 h	194	120	< 0.001
Respiratory rate (bpm)	Prior to NHF	28	32	0.778
	2 h	25	28	0.023
	6 h	24	26	0.003
	12 h	23	26	< 0.001
	18 h	22	25	0.001
	24 h	21	24	0.004
ROX index	Prior to NHF	5.81	4.06	0.169
	2 h	5.71	4.43	0.001
	6 h	6.55	4.86	< 0.001
	12 h	7.53	4.78	< 0.001
	18 h	8.6	5.10	< 0.001
	24 h	8.68	5.05	< 0.001

In those who had success, a higher ROX and SpO_2/FiO_2 versus lower RR were observed after and throughout the study.

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Results

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ROX score margin for failure over time

HOURS OF NHF USE	ROX SCORE FOR FAILURE	AUROC	POSITIVE PREDICTIVE VALUE %
2	< 2.85	0.679	98
6	< 3.47	0.703	98 – 99
12	< 3.85	0.759	99
> 12	< 4.88	NA	80

The prediction accuracy of the ROX index increased over time.

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Results

Hospital and ICU mortality and length of stay (LOS)

	SUCCESS N=123	FAILURE N=68	P-VALUE
ICU mortality	6 (4.9%)	29 (43.3%)	<0.001
Hospital mortality	17 (14.3%)	33 (51.6%)	<0.001
ICU LOS	6 (4 – 9)	20 (10 – 28)	<0.001
Hospital LOS	17 (11 – 29)	35 (23 – 65)	0.002

Those who succeeded on NHF therapy had lower rates of mortality and length of stay.

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Results

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- 35.6 % (N=68) participants failed, requiring intubation.
- Median duration success: 96h (48 – 144 hours) (P=0.001).
- Median duration failure: 24h (12 – 60 hours) (P<0.001).
- The prediction accuracy of the ROX index increased overtime.
- Participants with NHF failure presented a lower increase in the values of the ROX index over 12 hours.
- In those who had success, a higher ROX, SpO_2/FiO_2 and lower RR were observed after and throughout the study.
- ROX index < 2.85 at 2h, < 3.47 at 6h, and <3.85 at 12h post NHF initiation were predictors of failure.
- ROX index ≥ 4.88 for success was validated at three time points, in addition to the one first described (Roca, 2016).

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Conclusions

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- The ROX index can help to predict the outcome of NHF therapy in patients with AHRF due to pneumonia.
- A ROX index of ≥ 4.88, measured at 2, 6, or 12 hours, is a determinant of NHF success.
- ROX index values were identified and validated for three different time points which can predict NHF failure.
- Among measured components, SpO_2/FiO_2 had a greater predictive weight than RR.
- The index is dynamic and can be measured with ease and repetition at the patient's bedside.

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Notes

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- Adult pneumonia patients AHRF only.
- AIRVO™ 2 or MR850 used.

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Additional resources

- PubMed link

  www.ncbi.nlm.nih.gov/pubmed/30576221

- Full paper not freely available

- Clinical summary

- Clinical trial register

  www.clinicaltrials.gov, ID: NCT02845128

- ROC explained

  www.youtube.com/watch?v=21Igj5Pr6u4

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Glossary

AUROC:
Area under receiver operating curve.

ROC:
A receiver operating characteristic curve or ROC curve, is a plot illustrating the diagnosticability of a binary classifier system as its discrimination threshold is varied.

HR:
Hazard ratio is the ratio of (chance of an event occurring in the treatment arm)/(chance of an event occurring in the control arm). The HR has also been defined as the ratio of (risk of outcome in one group)/(risk of outcome in another group), occurring at a given interval of time.

COX PROPORTIONAL HAZARDS MODELING:
Cox regression (or proportional hazards regression) is the method for investigating the effect of several variables upon the time a specified event takes to happen.

RR:
Respiratory rate.

Roca et al. *Am J Respir Crit Care Med*. 2018 [Epub ahead of print].