

Predictors of Non-invasive Ventilation Response Do Not Indicate Response to High Flow Nasal Oxygen: A Bicentric Observational Study.

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Abstract

Background

In patients receiving high flow nasal oxygen (HFNO), predicting chance of response is crucial in order to avoid unnecessary delay of intubation. Whether commonly used predictors of non-invasive ventilation (NIV) response may be as applicable for HFNO, is unclear.

Methods

We conducted a retrospective bi-centric analysis of adults treated with HFNO in two Austrian medical intensive care units from 01/2014 until 09/2017. Predictive value of respiratory rate, PaO₂, PaCO₂, SpO₂, ROX index, pH, heart rate, base excess, SOFA-Score and SAPS III was analysed by means of logistic regression with HFNO responding as dependent variable. Calculations were also done separately in patients receiving HFNO as post-extubation support (Group A) and all other indications (Group B).

Results

We registered 127 patients (m:f = 70:57, median age: 67 [IQR 53-77] years). Forty-eight patients (37.8%) received HFNO as post-extubation support and were assigned to group A. Seventy-nine patients (62.2%) received HFNO due to any other indication and were assigned to group B. Criteria of HFNO response were fulfilled by 42 patients (87.5%) of group A and 53 (67.1%) of group B patients.

Whereas respiratory rate, PaO₂, PaCO₂, SpO₂, pH, heart rate, base excess, SOFA-Score and SAPS III did not differ between responders and non-responders, ROX index showed significant association with HFNO success in all patients. With increasing ROX index, the odds for response increased (OR [95% CI]: baseline: 1.21 [1.05, 1.38], p = 0.0069, after 2 hours: 1.19 [1.05; 1.34], p = 0.0061, after 6 hours: 1.23 [1.06; 1.42], p = 0.0049). Subgroup analyses revealed similar odds ratios for ROX index (baseline: group A: 1.17 [0.90; 1.52], p = 0.24; group B: 1.22 [1.04; 1.43], p = 0.015; after 2 hours: 1.30 [0.94; 1.82], p = 0.12, group B: 1.18 [1.03; 1.34], p = 0.014; after 6 hours: 1.76 [1.01; 3.06], p = 0.047, group B: 1.19 [1.03; 1.37], p = 0.022).

Conclusions

Criteria of HFNO success deviate from criteria for response to NIV. ROX index indicated HFNO response in a wide range of indications.

Background

During the last decade, high flow nasal oxygen (HFNO) has steadily regained importance as a treatment for acute respiratory failure (ARF) in adults. Current devices generate O₂ flow rates of up to 60 L/min allowing for a considerable washout of nasopharyngeal dead space and application of mild continuous positive airway pressures (CPAP) (1–3). Furthermore, warming and humidification of the inspired air as

well as special high flow nasal cannulas (HFNC) with pliable nasal prongs improve patient's comfort and mucociliary clearance when compared to standard low-flow nasal oxygen administration (4–6). Several studies consequently report the improvement of oxygenation as well as clinical condition in hypoxemic patients receiving HFNO (2, 7–10). Whether these clinical benefits translate into relevant prolongations of survival, reductions in length of ICU stay, or reduced intubation rates is unknown. Literature rather gives cause for concerns whether HFNO therapy could prolong the decision making process when in fact invasive mechanical ventilation is inevitable (11). In patients receiving non-invasive ventilation (NIV) by means of CPAP, early changes in vital parameters such as pH, PaCO₂ or respiratory rate (RR) allow for early estimation of response (12–15). In patients treated with HFNO, criteria for anticipating therapy success such as ROX index (16) are scarce and setting the timing for intubation is challenging.

The aim of the present work is to describe a patient population receiving HFNO in two Austrian intensive care units (ICUs) and to elucidate suitable values for therapy response.

Methods

Study design and setting

This bi-centric, retrospective, observational study was performed in the ICUs of the Department of Medicine I, General Hospital Vienna, Medical University of Vienna, Vienna, Austria (centre 1) and the Department of Medicine I, St. Joseph's Hospital Braunau, Braunau, Austria (centre 2). Centre 1 represents an 8-bed medical ICU of a tertiary care university-affiliated hospital, centre 2 is a 6-bed medical ICU of a national certified academic teaching hospital. Both centres are led by and staffed with specialists in medicine with supra-speciality in intensive care medicine offering a considerable experience in the treatment with HFNO.

Selection of participants and data collection

We included all patients ≥ 18 years treated with HFNO between 01/2014 and 09/2017 in the above-mentioned ICUs. Patient identification and data were gathered from both the patient data management systems and the local laboratory databases.

The prospectively done routine documentation included demographic data of patients, underlying disease, reason for admission, vital parameters, indication for HFNO, reason for end of HFNO (e.g. improvement / worsening of respiratory condition), duration of HFNO as well as complications during the course of the therapy. Routine blood chemistry and blood cell count were documented on a daily basis. Vital signs and arterial blood gas analysis values were routinely documented and collected before (baseline), 2h after and 6h after HFNO initiation. Device related parameters such as gas flow, fraction of inspired oxygen (FiO₂) or temperature of inspired air were documented on a regular basis. We retrospectively calculated sequential organ failure (SOFA) score (17), simplified acute physiology score 3 (SAPS III) (18) upon admission and prior to HFNO start. Moreover, we calculated ROX Index (16) defined

as the ratio of defined as the ratio of peripheral O₂ saturation (SpO₂) / FiO₂ over respiratory rate (RR) at baseline, 2h and 6h after HFNO initiation.

In both centres Airvo™ 2 system was used for HFNO treatment comprising Optiflow™ nasal interface (Fisher & Paykel Healthcare Corporation Limited, Auckland, New Zealand). Airvo™ 2 is a widely used humidifying high flow system with a built-in flow generator allowing for a gas flow range of 2 to 60 L/min. We regarded RR, PaO₂, PaCO₂, SpO₂, pH, heart rate (HR), base excess (BE) and ROX Index as possible predictors.

The study protocol was approved by the local ethical review boards of both Medical University of Vienna and Upper Austria according to Austrian law regulations (EK No: 1003/2017).

Groups A and B

We analysed all included patients irrespective of HFNO indication. To address the different aetiology and pathogenesis of post-extubation respiratory failure and primary arising ARF, however, a distinction was drawn between HFNO for post-extubation management (group A) and HFNO for primary therapeutic strategy (group B).

Definition of response

All patients ultimately weaned from HFNO and switched to room air or low-flow O₂ administration via Venturi mask or standard nasal cannula, respectively, were defined as responders. Escalation to NIV or intubation with mechanical ventilation as well as death during HFNO therapy was regarded non-responding.

Statistical analysis

Quantitative variables are reported as median (first quartile – third quartile) if not stated otherwise. For qualitative variables, the absolute frequencies and percentages are reported.

The duration of HFNO was plotted by cumulative incidence curves (event of interest: End of HFNO due to response, competing event: End of HFNO due to non-response or death) for the two subgroups (group A / group B) separately.

Univariate logistic regression models were calculated with „HFNO responding“ as the dependent variable. The odds ratio (OR) with 95% confidence limits and the p-value (H0: OR = 1) are reported. Graphical visualization was done by boxplots for responders and non-responders separately.

For analyses of baseline predictors, all patients were included. For analyses of predictors at the time of 2h (or 6h), only those patients with HFNO-duration > 2 h (or > 6 h) were included.

To illustrate the diagnostic ability of ROX index, we used receiver operating characteristic curves (ROC). An AUC between 0.7 and 0.8 was regarded as “acceptable discrimination”. For ROX at baseline, the cut-off with the maximal Youden-index (Youden-index = sensitivity + specificity – 1) was selected (17). For this cut-off, sensitivity and specificity with 95% Clopper-Pearson confidence limits are reported.

Differences with a p less than 0.05 were considered statistically significant. The number of invalid values is stated within the respective tables. Due to the exploratory character of the study and in favour of the crucial distinction between group A and group B, we did not adjust for multiple testing. Calculations were performed by a statistics software package (R 3.6.2., GNU GPL and IBM SPSS Statistics, IBM, Armonk, New York). The datasets generated during and / or analysed during the current study are available on reasonable request.

Results

Descriptive statistics

During the study period, 127 patients (m:f = 70:57, median age: 67 [IQR 53-77] years) treated with HFNO were registered in both centres (centre 1: 61 patients, centre 2: 66 patients). Of all patients, 79 (62.2%) had an underlying pulmonary diagnosis at the time of hospital admission. In 63 cases (49.6%), reason for ICU admission was respiratory failure.

Forty-eight patients (37.8%) received HFNO as post-extubation support and were assigned to group A. Seventy-nine patients (62.2%) received HFNO due to respiratory failure and were assigned to group B. Neither mortality risk, expressed by SOFA-Score, nor severity of illness, expressed by SAPS III, showed significant differences between responders and non-responders. Patient characteristics are shown in Table 1.

Table 1
Patient characteristics.

		Group A responder		Group A non - responder		Group B responder		Group B non - responder	
		n	(%)	n	(%)	n	(%)	n	(%)
		42		6		53		26	
Reason for admission	Cardiovascular	12	(29%)	0	(0%)	6	(11%)	4	(15%)
	Infection/sepsis	12	(29%)	1	(17%)	8	(15%)	10	(39%)
	Respiratory	16	(38%)	5	(83%)	31	(59%)	11	(42%)
	Monitoring	2	(5%)	0	(0%)	8	(15%)	1	(4%)
Underlying respiratory illness		26	(62%)	3	(50%)	37	(70%)	13	(50%)
Indication for HFNO	Postextubation support	42	(100%)	6	(100%)	0	(0%)	0	(0%)
	Respiratory failure	0	(0%)	0	(0%)	53	(100%)	26	(100%)
Male Sex		19	(45%)	5	(83%)	31	(58%)	15	(58%)
Age		69		71		64		67	
		(51-77)		(47-75)		(55-76)		(58-78)	
Mortality risk	SOFA-Score	7		10		6		7	
		(5-10)		(7-12)		(5-8)		(5-11)	
Severity of illness	SAPS III	52		49		50		51	
		(42-57)		(45-56)		(44-56)		(43-59)	

Data are given as median and interquartile range or numbers and percent.

ICU intensive care unit, HFNO high flow nasal oxygen, NIV non-invasive ventilation, SOFA Sequential Organ Failure Assessment, SAPS Simplified Acute Physiology Score

Group A

All group A patients (n=48) received HFNO immediately after extubation, of whom 42 (87.5%) were weaned ultimately from O₂ support and thus fulfilled criteria for therapy response. Thirty-nine of all

responders in this group were directly switched to nasal low-flow oxygen administration, one needed O₂ via Venturi mask and two did not receive any oxygen support following HFNO, respectively. Six patients were HFNO non-responders, of whom three patients died as therapy limitation included the decision not to apply mechanical ventilation again. The three remaining patients received endotracheal re-intubation due to hypercapnia despite full HFNO support. Primary reason for intubation was progressive respiratory failure in 21 patients (43.8%), impaired neurology in 13 patients (27.1%), acute heart failure in twelve patients (25.0%) and others in two patients (4.8%). Indication for HFNO was presumed high risk of post-extubation respiratory failure according to the clinicians' opinion.

Group B

In Group B all patients (n=79) received HFNO due to primary respiratory failure, of whom 53 (67.1%) were weaned ultimately from any O₂ support and thus fulfilled our criteria for HFNO responding. Indication for HFNO was respiratory failure in 79 patients (100%). Three patients in group B were eligible for NIV due to leading hypercapnia but poorly tolerated CPAP interface. Of all responders in this group, 46 patients were switched to low-flow nasal O₂, 6 patients needed O₂ via Venturi mask and one did not receive any oxygen support following HFNO. Twenty-six patients (32.9%) of group B were categorised non-responders, of whom six were switched to NIV and 13 required intubation with mechanical ventilation due to progressive hypoxia, respectively. Seven patients died during ongoing HFNO treatment due to therapy withdrawal. Plots of HFNO duration by cumulative incidence curves of all patients are shown in figure 1.

Univariate logistic regressions

For group B patients, the odds of response was lower compared to patients in group A (OR [95% CI]: 0.29 [0.11; 0.77]). At baseline, there were no significant differences in the other variables RR, PaO₂, PaCO₂, SpO₂, pH, heart rate (HR), BE, SOFA-Score or SAPS III (Table 2). Results of the univariate logistic regression models separated into group A and group B, respectively, showed no significant differences.

Table 2
Results of the univariate logistic regression models with odds ratios (OR) of HFNO response, baseline variables, all patients.

Variable	estimate	OR	95% LL	95% UL	p-value	n NR/ n R	unit
RR	-0.0436	0.9574	0.9063	1.0113	0.1195	24/ 89	1
PaO ₂	0.0079	1.0079	0.9765	1.0403	0.6249	24/ 90	1
PaCO ₂	0.0108	1.0109	0.9784	1.0444	0.5161	24/ 90	1
SpO ₂	0.0092	1.0093	0.9482	1.0743	0.7718	26/ 90	1
pH	0.1363	1.1461	0.6832	1.9226	0.6055	24/ 90	0.1
Group A	-1.2337	0.2912	0.1098	0.7726	0.0132*	32/ 95	1
HR	-0.0155	0.9846	0.9622	1.0075	0.1861	26/ 90	1
BE	0.0691	1.0716	0.9914	1.1583	0.0815	24/ 90	1
SOFA Score	-0.1099	0.896	0.785	1.0226	0.1034	25/ 90	1
SAPS-III	-0.0111	0.9889	0.9497	1.0298	0.5905	32/ 95	1

HFNO high flow nasal oxygen, RR respiratory rate, PaO₂ arterial oxygen partial pressure, PaCO₂ arterial carbon dioxide partial pressure, SpO₂ peripheral oxygen saturation, HR heart rate, BE base excess, SOFA Sequential Organ Failure Assessment, SAPS Simplified Acute Physiology Score. Asterisks denote statistical significance.

Difference of predictors between baseline and 2h after HFNO start (Δ RR, Δ PaO₂, Δ PaCO₂, Δ SpO₂, Δ pH, Δ HR and Δ BE) showed no significant difference in all patients as well as within the two subgroups (Additional Table 1a and 1b).

Difference of predictors between baseline and 6h after HFNO start (Δ RR, Δ PaO₂, Δ PaCO₂, Δ SpO₂, Δ pH, Δ HR and Δ BE) showed no significant difference in all patients as well as within the two subgroups (Additional Table 2a and 2b).

In all patients, the effect of ROX on response was statistically significant at baseline ($p = 0.0069$), after 2h ($p = 0.0061$) and after 6h ($p = 0.0049$). If increasing ROX at baseline by 1, the odds of response increased by the factor 1.21 [1.05; 1.38]. Details are shown in Table 3. ROC curves of ROX at baseline, after 2h and after 6h, respectively, are shown in figure 2, figure 3 and figure 4. The best-cutoff according to the Youden-index of ROX baseline was 8.578. If categorizing patients with ROX baseline ≥ 8.578 as responders and patients < 8.578 as non-responders, the sensitivity [95% CI] would be 0.674 [0.567; 0.77] and the specificity [95% CI] 0.696 [0.471; 0.868].

Table 3

Results of the univariate logistic regression models of ROX index values with odds ratios (OR) of HFNO response, all patients.

Variable	estimate	OR	95% LL	95% UL	p-value	n NR/ n R	unit
ROX baseline	0.1886	1.2075	1.053	1.3847	0.0069*	23/ 89	1
FiO ₂ baseline	-0.0477	0.9534	0.9232	0.9846	0.0037*	24/ 90	1
SpO ₂ /FiO ₂ baseline	0.009	1.0091	1.002	1.0161	0.0115*	24/ 90	1
ROX 2h	0.1713	1.1869	1.05	1.3416	0.0061*	28/ 90	1
FiO ₂ 2h	-0.0298	0.9706	0.9499	0.9918	0.0068*	30/ 92	1
SpO ₂ /FiO ₂ 2h	0.0069	1.0069	1.0009	1.0129	0.0235*	30/ 92	1
ROX 6h	0.2059	1.2286	1.0645	1.4181	0.0049*	22/ 83	1
FiO ₂ 6h	-0.0353	0.9653	0.9417	0.9895	0.0052*	25/ 89	1
SpO ₂ /FiO ₂ 6h	0.0143	1.0144	1.0056	1.0233	0.0012*	22/ 87	1

SpO₂ peripheral oxygen saturation, FiO₂ fraction of inspired oxygen, LL lower limit, UL upper limit, NR non-responder, R responder. Asterisks denote statistical significance.

The subset analysis of ROX in group A shows borderline significance after 6h (Additional Table 3). Within group B, ROX showed significant correlation to response at baseline as well as after 2h and 6h, respectively (Additional table 4). Boxplots of ROX index as well as absolute frequencies are shown in figure 5 and Additional table 5, respectively.

Discussion

NIV criteria

In our bi-centric retrospective analysis of 127 patients, commonly utilized criteria for NIV response such as RR, PaO₂, PaCO₂, HR, or pH (12–15, 18) did not show significant association with HFNO therapy responding during the first hours of use. This is shown for absolute values as well as for differences between baseline and 2h or 6h. Indeed, several other variables such as severity of disease, oxygenation, thoracoabdominal asynchrony or need for vasopressors have been shown to be associated with HFNO response (2, 19–21). Since directly predictive association of these variables has never been verified, clinicians administering HFNO are merely advised to closely monitor the same indicators as mentioned above for NIV responding including respiratory pattern and oxygenation in order to promptly detect the

necessity for invasive mechanical ventilation, although the principles of HFNO and NIV considerably differ (10).

Our findings support the hypothesis that the use of the abovementioned NIV response criteria might not be suitable for patients receiving HFNO.

ROX index

Roca et al. described ROX Index defined as the ratio of SpO_2 / FiO_2 to RR. To date, it is the only prospectively validated tool for prediction of HFNO success. In this selected population, patients with a ROX index ≥ 4.88 after 12 h of HFNO had higher chances of responding with no need for mechanical ventilation (16, 22). In our univariate logistic regression models, the effect of ROX on HFNO response was significant at baseline, after 2h and after 6h, respectively. The area under the curve (AUC) was between 0.7 and 0.8 in all time points, assuming acceptable discrimination according to the criteria of Hosmer and Lemeshow (23). The best-cutoff at baseline was selected according to the Youden-index (17). It has to be noted that the confidence intervals are wide. These values need to be put into a descriptive perspective in order to allow for comparability of cutoff values in future studies. Furthermore, it has to be emphasized, that ROX was originally validated for pneumonia-related hypoxemic respiratory failure, whereas in our patient population, reasons for HFNO substantially varied. Considering pneumonia as a major cause of respiratory failure, however, our findings are in line with late-breaking literature that suggests the use of an algorithm using the time course of ROX index from 2h, 6h and 12h, respectively (24). In our population, the effect of ROX index on response showed significant levels starting from baseline. This finding raises the question, whether ROX index may have predictive value as early as with the beginning of HFNO, i.e. reading the first values after therapy start. However, randomized controlled trials are needed in order to compare this suggestion with standard of care and to expand reporting to respiratory failure of other causes.

Group A

To address the different aetiology and pathogenesis of post-extubation respiratory failure and primary arising ARF, a distinction was drawn between HFNO for post-extubation management (group A) and HFNO for primary therapeutic strategy (group B).

In group A six of 48 patients (12.5%) were regarded non-responders which resembles the current literature's re-intubation rate following planned extubation of 12 to 14% (25–27). Apart from a borderline significant OR of ROX 6h after HFNO start ($p=0.047$), no significant changes were found during the time course. However, performance of ROX in patients following extubation remains to be elucidated. Moreover, the case number of group A non-responders in our study is as low as 6. Even though these findings have limited informative value due to the small cohort, the clinical threshold of utilizing HFNO following extubation could be lowered due to the obviously high chance of response in this group.

Same as NIV, HFNO is not generally recommended following extubation as a preventative measure against reintubation. The patient population deemed at risk of postextubation respiratory failure, however, may benefit from extubation directly to subsequent HFNO. Since this risk assessment is often based on rather informal criteria such as weak cough, frequent suctioning or positive fluid balance during the 24 hours before extubation, clinical practice varies considerably. Decision is usually individualized taking type of respiratory failure and oxygen demand into account (28).

HFNO as a reintubation prophylaxis has formally been evaluated in few randomized clinical trials hypothesising non-inferiority of HFNO compared to NIV at least in surgical cohorts (29). However, data to support the use of HFNO for post-extubation management of adult patients are limited and do not support its routine application. Furthermore, our study population did not comprise postoperative patients.

Interestingly, all three non-responders receiving reintubation were hypercapnic at this time. This observation may emphasize the limitation of HFNO in patients with predominant hypercapnic respiratory failure. Even though mortality rates may be equal, patient populations with underlying obstructive pulmonary disorders are possibly more likely to benefit from immediate NIV following extubation rather than from HFNO (30, 31).

Group B

Group B comprises patients treated with HFNO due to all reasons except for post-extubation management. In group B, the non-responder rate of 32.9% approximately corresponds to the current literature's intubation rates of 35% for patients with severe hypoxemia treated with HFNO (8). Non-responders showed no significant changes of RR, PaO₂, PaCO₂, SpO₂, HR, BE or pH after 2 and 6 h of HFNO start compared to baseline. Less expected, also responders showed no significant differences in these values. Similar to our analysis in all patients (see above), ROX index showed a significant effect on response in all time points including baseline.

These findings underline that prediction of NIV and prediction of HFNO success should be distinguished irrespective of HFNO indication. Even when excluding our patient population with HFNO for post extubation support (group A), only ROX index showed significant values. However, the number of group B patients in this population is as low as 79, of which only 26 are non-responders. Observed differences between responders and non-responders in this group may be caused by this unequal number of cases which is why our findings need to be challenged.

Three patients in group B were eligible for NIV due to leading hypercapnia but poorly tolerated NIV. One of its major disadvantages compared to HFNO is common intolerance of CPAP interface or ventilation which often leads to progressive respiratory distress. Similar to all other patients in our population, high flow oxygen delivery via HFNO was tolerated well.

Seven of the group B non-responders died during ongoing HFNO due to therapy withdrawal. Similar to group A, potential responding of these patients in case therapy would have been continued may be undetected.

Strengths and limitations

Possible strengths of our study comprise its topicality in times of broad utilization and simultaneous high demands of HFNO, its focus on risk stratification including commonly used NIV-response predicting parameters and ROX, its bi-centric study design with relatively homogenous cohorts as well as the distinction between the two HFNO indications by means of subgroups A and B.

First limitation is with the retrospective character of the study and a rather small absolute patient number in each of the respective groups. Indeed, the merit of this deliberate design choice is to allow for differentiation of post-extubation support and primary ARF therapy. However, this results in insufficient data to perform multivariable analysis with adjustments for multiple testing with adequate power. Noticeably, this also includes correction for possible confounders such as the centre effect. Second, death during ongoing HFNO (n=10) was considered non-responding in order to avoid overestimation of therapy success. It has to be stressed, that these patients were a priori not considered eligible to further escalation of support. Third, the timing for the evaluation of therapy response is hardly assessable by retrospective studies and therefore not provided. Whether there was enough time between the detection of predictors and treatment response to make sure they are "predictors" rather than "indicators" of treatment failure, is not derivable from this data. Fourth, some values are missing due to the retrospective nature of the study possibly limiting significance and informative value. Fifth, the bi-centric design does not ensure generalizability of the study results.

Conclusion

In our patient population receiving HFNO due to respiratory failure or following extubation, ROX index has shown to be associated with HFNO success even in the early treatment phase. Commonly used criteria for NIV, however, did not predict therapy response. Further investigations are needed in order to elucidate its cut-off values and performance in different aetiologies.

Abbreviations

HFNO	high flow nasal oxygen
ARF	acute respiratory failure
CPAP	continuous positive airway pressure
HFNC	high flow nasal cannula
ICU	intensive care unit

NIV	non-invasive ventilation
RR	respiratory rate
FiO ₂	fraction of inspired oxygen
SOFA	simplified organ failure assessment
SAPS III	simplified acute physiology score III
HR	heart rate
BE	base excess

Declarations

Ethics approval and consent to participate

Informed consent statements are not required. The study protocol was approved by the local ethical review boards of both Medical University of Vienna and Upper Austria according to Austrian law regulations (EK No: 1003/2017).

Consent for publication

Not applicable.

Availability of data and materials

The datasets generated during and / or analysed during the current study are available on reasonable request.

Competing interests

TS is member of the Xenios medical advisory board and received speaker fees from Getinge, Baxter and Xenios. PS has received speaker fees by Maquet and a Horizon 2020 Fast Track to Innovation Grant by the European Commission (NCT04115709).

The remaining authors declare no conflicts of interest.

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Authors' contributions

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Figures

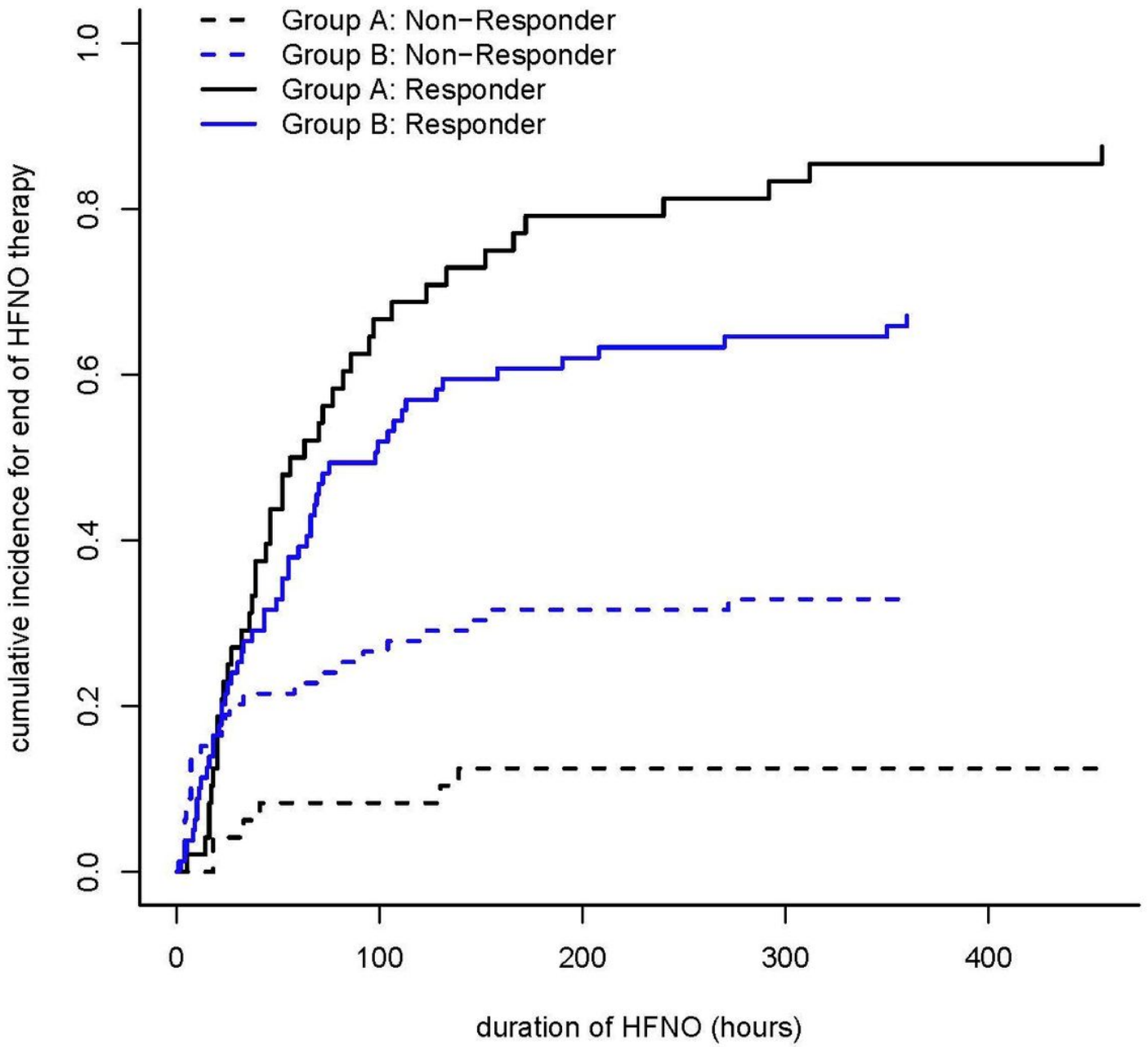


Figure 1

Cumulative incidence curves for the two subgroups (group A, group B). HFNO high flow nasal oxygen

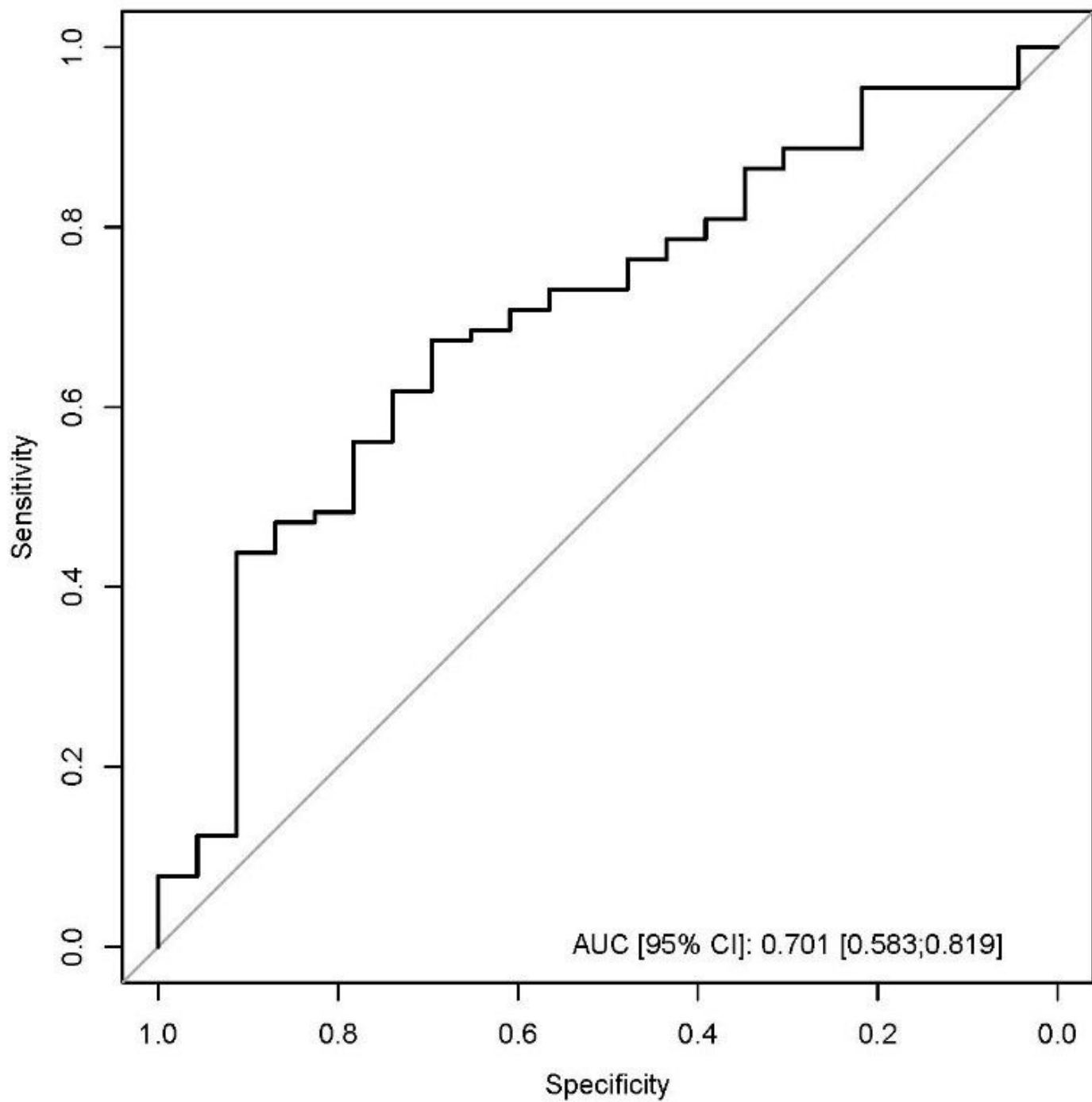


Figure 2

Receiver operating characteristic (ROC) curve of ROX index on HFNO response at baseline, all patients. HFNO high flow nasal oxygen

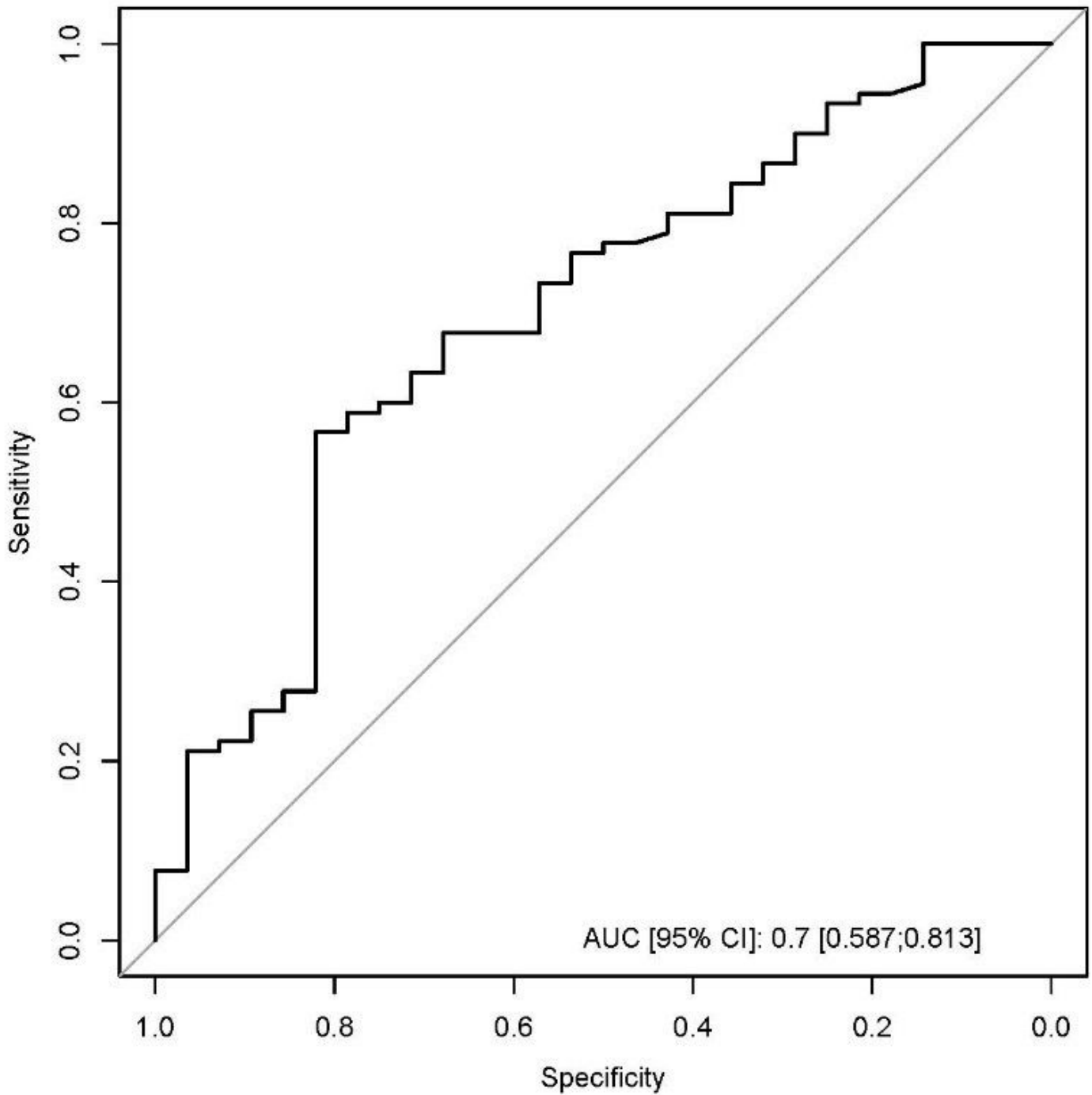


Figure 3

Receiver operating characteristic (ROC) curve of ROX index on HFNO response after 2h, all patients. HFNO high flow nasal oxygen

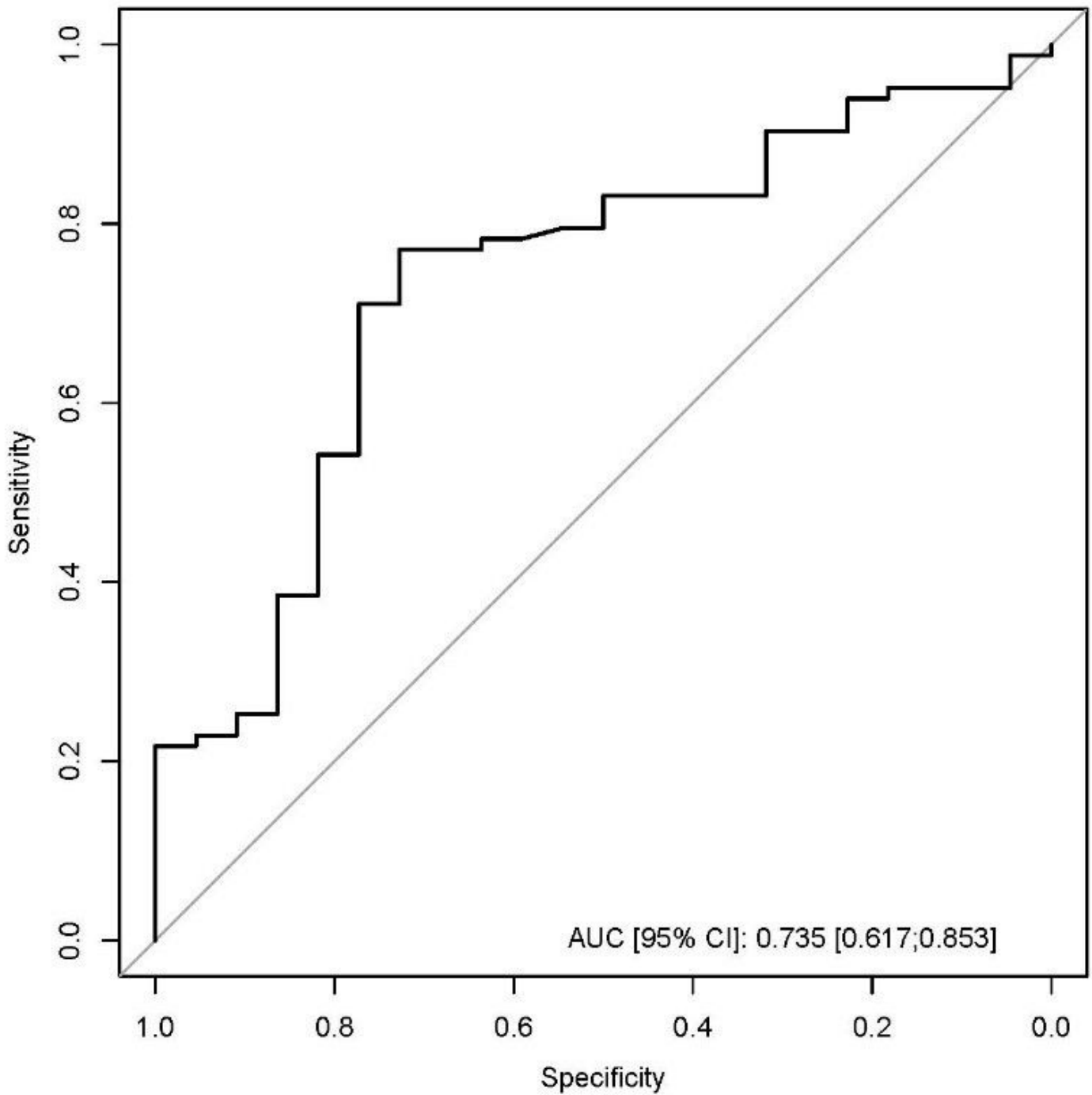


Figure 4

Receiver operating characteristic (ROC) curve of ROX index on HFNO response after 6h, all patients. HFNO high flow nasal oxygen

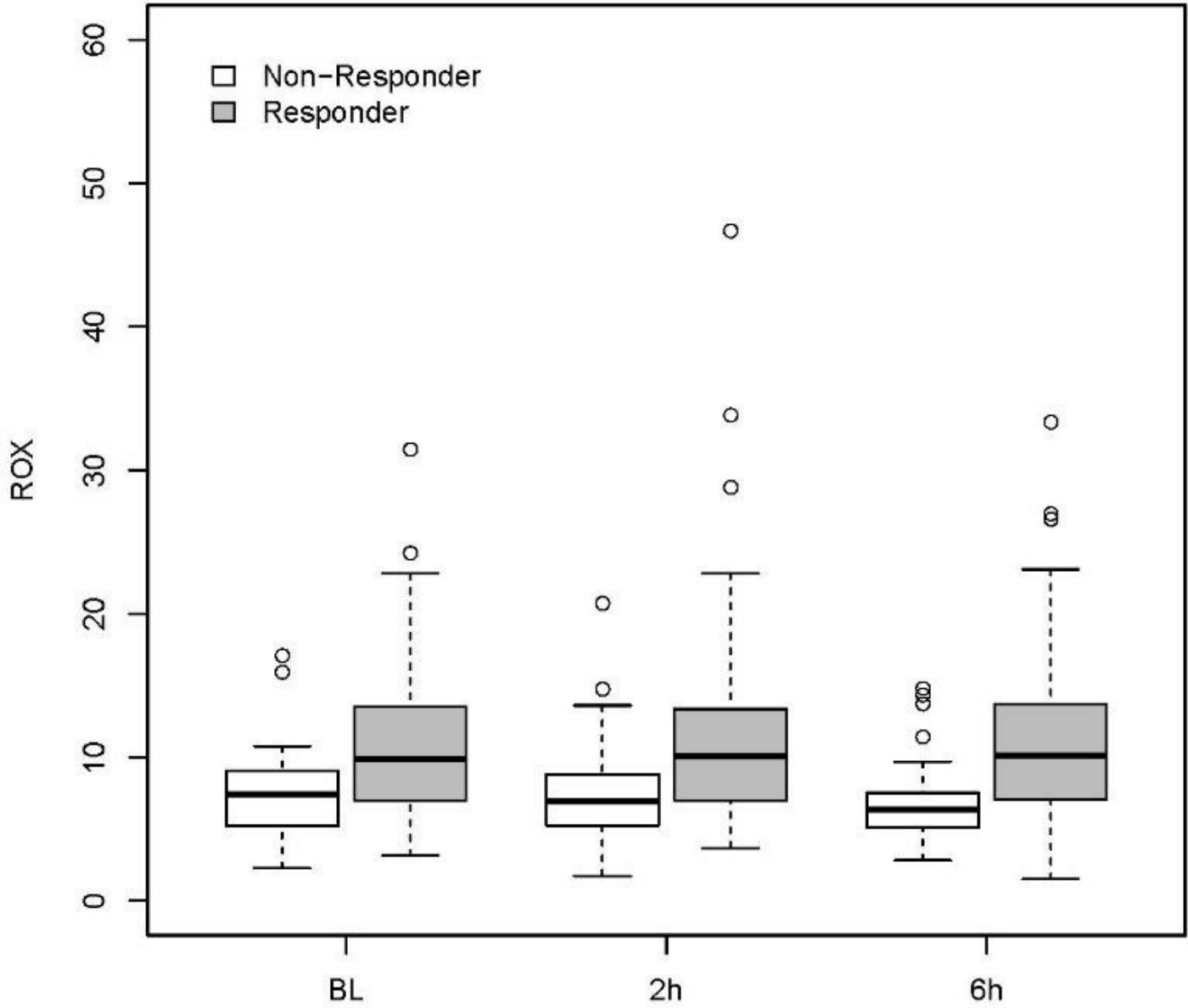


Figure 5

Boxplots of ROX index during the time course of HFNO therapy. HFNO high flow nasal oxygen

Supplementary Files

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