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# **Outcome of Noninvasive Ventilation in Acute Respiratory Failure**

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### **ABSTRACT**

## **Background**

Noninvasive ventilation (NIV) represents the delivery of positive pressure to the lungs without inserting an endotracheal tube. Noninvasive ventilation has been successfully used in patients with acute respiratory failure. There is a tremendous increase in usage of NIV in clinical settings aiming to reduce complications due to invasive ventilation and to improve resource utilization. It is imperative to watch for outcome of NIV in patients with acute respiratory failure.

#### Materials and methods

A total of 50 patients were included in this prospective longitudinal study and divided into two groups: type I and type II respiratory failure. All patients were administered bilevel positive airway pressure (BIPAP) ventilator support system using full-face mask or nasal mask depending on the status of the patient. Dyspnea quantitated by modified Borg dyspnea score, heart rate (HR), respiratory rate (RR), blood pressure, and arterial blood gas analysis were assessed at the end of 4, 12, and 24 hours.

### Results

Respiratory rate and HR were significantly improved at the end of 4, 12, and 24 hours with NIPPV compared with baseline (0 hour) in both groups (p < 0.01). Statistically significant improvements in pH and PaO<sub>2</sub> was seen with NIPPV at the end of 12 hours and 24 hours (p < 0.001) compared with the baseline in both type I and type II respiratory failure patients. Dryness of mouth and nose was noted in 3 (6.81%) patients with NIPPV.

### Conclusion

Study indicates that a trial of BIPAP is effective in improving gas exchange, reducing intubation, and length of stay in hospital in patients with acute respiratory failure.

### How to cite this article

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**Keywords:** Acute respiratory failure, Noninvasive ventilation, Outcome, Predictors

## INTRODUCTION

Noninvasive ventilation (NIV) refers to the delivery of positive pressure to the lungs without inserting an endotracheal tube. Noninvasive ventilation includes delivery of continuous positive airway pressure (CPAP) and all modalities of pressure controlled mechanical ventilation [noninvasive positive pressure ventilation (NIPPV)]. \( \frac{1}{2} \)

Noninvasive ventilation has been effectively applied in patients with acute respiratory failure with a significant reduction in mortality rate, need for endotracheal intubation, and length of stay compared with standard therapy. Noninvasive ventilation is widely used to treat acute respiratory failure due to different etiologies. The advantages of NIV over endotracheal intubation are obvious. Speech, airway defense mechanisms and swallowing functions are left intact. Trauma to the trachea and larynx is avoided; and patient comfort may be slightly improved.

Respiratory failure is defined as a failure to sustain adequate gas exchange and is characterized by abnormalities of arterial blood gas tensions. There are two types of respiratory failure—type I respiratory failure is defined by arterial  $PO_2$  ( $PaO_2$ ) of <8 kPa (60 mm Hg) with normal or low arterial  $PCO_2$  ( $PaCO_2$ ). Type II respiratory failure is defined by  $PaO_2$  of <8 kPa (60 mm Hg) and  $PaCO_2$  of >6 kPa (45 mm Hg).  $\frac{4.5}{2}$ 

Acute respiratory failure is usually characterized by life-threatening derangements in arterial blood gases and acid—base status. Acute respiratory failure may be classified as hypercapnic or hypoxemic. Hypercapnic and hypoxemic respiratory failure is defined as PaCO<sub>2</sub> greater than 45 mm Hg and PaO<sub>2</sub> less than 55 mm Hg, respectively, when the fraction of oxygen in inspired air (FiO<sub>2</sub>) is 0.60 or greater. <sup>6</sup>

Most of the studies published till date have shown encouraging results with the use of NIPPV in patients with acute respiratory failure. With NIPPV, the necessity for intubation has declined and the respiratory rate (RR) and gas exchange have been improved rapidly. It has been proved that NIPPV was linked with a reduced need for invasive mechanical ventilation, decreased mortality, and shorter hospital stay. 7,8

According to study by Lin et al., improved RR, especially during the first 30 minutes after the application of NIV treatment was associated with a better patient outcomes. Whereas Conti et al. in 2015 reported that arterial pH was confirmed as useful indicator of the severity of respiratory failure but a weak prognostic factor.

Although NIV has been widely researched, there is still a paucity of literature. This modality of treatment assumes greater relevance, particularly when resources are limited. There has been a tremendous rise in the use of NIV in clinical settings targeting reduction in complications of invasive ventilation and improvement in resource utilization. It is vital to look for the outcome of NIV in patients with acute respiratory failure. Hence, present study was conducted with the following aims and objectives:

• To evaluate the utility of NIV in hypoxemic respiratory and hypercapnic respiratory failures.

• To study the predictors of outcome of NIV in acute respiratory failure due to primary pulmonary pathology.

## **MATERIALS AND METHODS**

This was a prospective longitudinal study conducted in 50 patients conducted in the Department of Respiratory Medicine at the tertiary care hospital after obtaining the approval from the Institutional Ethics Committee. Written informed consent was obtained from the patient or from close relative of the patient. Study was conducted from January 2016 to August 2017.

### **Inclusion Criteria**

- Patient with type I respiratory failure due to primary pulmonary pathology.
- Patient with type II respiratory failure due to primary pulmonary pathology.

### **Exclusion Criteria**

- Age <18 years.
- Respiratory failure due to nonpulmonary pathology.
- Impaired consciousness (Glasgow coma scale <10).
- Patients with contraindications of NIV.
- Severe upper gastrointestinal bleeding.
- Chest trauma.

The baseline evaluation consisting of demographic profile, clinical profile, family history, personal history, and medical diagnosis were recorded; and thorough clinical evaluation was conducted. Parameters recorded include dyspnea quantitated by modified Borg dyspnea score, heart rate (HR), RR, blood pressure, and arterial blood gas analysis. Routine investigations were done. Chest X-ray was performed.

All patients were administered BIPAP ventilator support system using full face mask or nasal mask depending on the patient's status. The initial trial parameters (in spontaneous mode) were 8 cm H<sub>2</sub>O of inspiratory positive airway pressure (IPAP) and 4 cm H<sub>2</sub>O of expiratory positive airway pressure (EPAP). The IPAP and EPAP parameters were titrated to optimize patient comfort. Both IPAP and EPAP were adjusted to a maximum of 24 and 12, respectively. The FiO<sub>2</sub> requirement was assessed as per arterial blood gas (ABG) analysis. BIPAP was applied to patients in bed at an angle of 30–45° by face mask or nasal mask. The standard disinfection protocol was followed for disinfection/sterilization of mask and tubing.<sup>4</sup>

Pressures were gradually increased by 2–5 cm H<sub>2</sub>O every 10 minutes to obtain oxygen saturation above 90% with monitoring of RR. Patients were clinically assessed every 15 minutes for the initial 2 hours. Each patient was continuously monitored for pulse rate, RR, respiratory distress, blood pressure, Glasgow Coma Scale, level of cooperation, mental status, oxygen saturation, and signs of air leakage around the mask. Standard medical treatment including inhalational drugs, intravenous corticosteroids, xanthines and whenever appropriate, antibiotics were given in addition to BIPAP.

Once stable settings were achieved, a posttrial ABG level was obtained in all patients after 4, 12, and 24 hours after initiation of NIV and whenever required to assess adequacy of ventilation. Heart rate, RR, and dyspnea using modified Borg scale were monitored at 4, 12, and 24 hours interval. BIPAP was given continuously for 24 hours and then depending on response, BIPAP was given intermittently and the duration was gradually reduced. If the patient improved within the initial 4 hours, NIV was continued and

clinical assessments were performed every 2 hourly until the patient was recovered from underlying respiratory failure. Daily clinical assessment ABG, were performed. Patients were followed until weaning from NIV and outcome was recorded as favorable. Those patients who required intubation and were started on mechanical ventilation anytime during the study were considered as NIV failure.<sup>4</sup>

If inspite of maximal NIV support and oxygen if patient's Glasgow Coma Scale deteriorated and if tachycardia, tachypnea, and respiratory distress did not improve, ABG was repeated after 1 hour of NIV treatment and decision was taken about endotracheal intubation and mechanical ventilation. <sup>7</sup>

Treatment with BIPAP was considered "Successful" if clinical and functional improvement had been achieved and "Failure" if the patient was intubated and started on mechanical ventilation.

The outcome of NIPPV usage was measured in terms of number of patients treated by NIPPV and those who failed on NIPPV. Other variables collected in the study included dyspnea score, RR, HR, ABG parameters (pH, PaCO<sub>2</sub>, and PaO<sub>2</sub>), mean duration of NIPPV application, the duration of hospital stay, and any complications related to the procedure if any. During the study, predictors were recorded, such as age, underlying comorbidity, HR, RR, oxygen saturation, and ABG (on admission).

# **Statistical Analysis**

The sample size (*n*) was calculated to be 49 assuming success rate with NIPPV as 85%, absolute precision as 10%, the desired confidence level of 95%. Hence, 50 patients were recruited during the study period.

Continuous variables were presented as mean  $\pm$  SD, categorical variables were expressed in frequency and percentages. Continuous variables were compared at a different time points by performing repeated measure analysis of variance (ANOVA) test. Changes in study parameters at 4, 12, and 24 hours from baseline between groups were compared by Mann–Whitney test for nonnormalized data and independent t test for normalized data. Categorical variables were compared using Pearson's Chi-square test. All the tests were two-sided. p < 0.05 was considered as statistical significance. Statistical software STATA version 14.0 was used for data analysis.

# **RESULTS**

Mean age of the population was  $56.16 \pm 12.7$  years. Most of the patients were in the age group of 61-70 years (34%) followed by 51-60 years (30%). A total 56% patients were men and 44% were women. Sex ratio was 14:11. Mean body mass index (BMI) of the study population was  $25.47 \pm 3.32$  kg/m<sup>2</sup>.

There were 68% patients from rural and 32% were from urban backgrounds. 58% patients were smokers; and 18% patients were exposed to biomass fuel in the study population. Patients with type I and type II acute respiratory failure were 32% and 68%, respectively.

Pulmonary diseases causing respiratory failure in the study population were chronic obstructive pulmonary disease (COPD) (46%) followed by pneumonia (24%), bronchiectasis (12%), post-tuberculosis (TB) sequele obstructive airway disease (OAD) (8%), interstitial lung disease (ILD) (6%), parapneumonic effusion (2%), and bronchial asthma (2%). On bacterial culture, growth was demonstrated in 20% of patients presenting with respiratory failure.

Out of 50 patients, who were administered NIPPV, 6 patients deteriorated and required intubation. Outcome of NIV is given in <u>Table 1</u>.

The mean modified Borg dyspnea score was significantly improved at the end of 4, 12, and 24 hours (p < 0.001) in both type I and type II respiratory failure patients.

The change in mean vital parameters at the different follow-up periods is given in <u>Table 2</u>. Mean change in arterial blood gas parameters at the different follow-up periods is given in <u>Table 3</u> and <u>Figure 1</u>.

The difference between the mean duration of NIV was not statistically significant for type I and type II respiratory failure patients. Also, it was found that there was no significant difference in the length of stay between the two groups.

Success was defined by the avoidance of endotracheal intubation with clinical and ABG improvement. Patients who did not improve clinically and on ABG parameters with NIPPV and needed intubation were considered as failure and were excluded from the study. However, these patients followed until recovery or death. Data of failure patients were available until 4 hours of starting NIPPV. Therefore, their clinical and ABG status was compared at baseline and at the end of 4 hours after starting NIPPV. Patients with multiple comorbidities had more NIV failure. Diabetes mellitus (p < 0.05) and renal disease (p < 0.001) were significantly associated with NIV failure. Comorbidities, such as pulmonary hypertension, hypertension and post TB sequel were not significant.

There was a significant improvement in breathing with NIPPV in both success and failure groups at the end of 4 hours compared with baseline. However, improvement in dyspnea scores in the success group was highly significant compared with the failure group (p = 0.0022).

Comparison of mean RR and HR at the end of 4 hours from baseline in success and failure and between groups is given in <u>Table 4</u>.

Improvement in pH, PaCO<sub>2</sub>, and PaO<sub>2</sub> after NIPPV in both success and failure groups at the end of 4 hours compared with baseline is depicted in <u>Table 5</u>.

### DISCUSSION

The present study was conducted to evaluate the utility of NIV and to study the predictors of outcome of NIV in acute respiratory failure.

Successful treatment with NIV was associated with an improvement in clinical parameters, such as modified Borg's dyspnea score, RR, HR, and arterial blood gas status. Endotracheal intubation was considered if patient did not improve after NIPPV trial.

The present study population consisted of 50 patients with a mean age of  $56.16 \pm 12.7$  years and a sex ratio of 14:11. Mean BMI of the study population was  $25.47 \pm 3.32$  kg/m<sup>2</sup>. Most of the patients were from rural areas (68%). In the present study, most common major underlying diseases were COPD (46%) followed by pneumonia, bronchiectasis, post-TB sequele OAD, ILD, parapneumonic effusion, and bronchial asthma. These findings were in accordance with the study by Lin et al.<sup>8</sup>

In the present study, BIPAP was found to be successful in causing rapid and sustained improvement in gas exchange in acute respiratory failure patients, both type I (87.5%) and type II (88.23%). In this study, 50 patients were given NIPPV and the overall efficacy of BIPAP in avoiding intubation was (88%). Similar results were reported by Ventrella et al. and George et al. in their studies stating that NIV was successful in (81%) and (85%) of patients with acute respiratory failure, respectively. 7.10

In the present study, BIPAP given to acute respiratory failure patients was not significantly different among type I and type II respiratory failure patients with respect to success/failure rates, the duration of NIV and length of stay in hospital suggesting that acute respiratory failure patients benefit with BIPAP irrespective of the type of failure. Thus, it is not important to differentiate between type I failure and type II respiratory failure to initiate BIPAP considering its 88% overall efficacy. The overall intubation rate of 12% compares favorably with failure rates of 15% in a study by George et al. in patients with acute respiratory failure with NIPPV. Kramer et al. reported that 31% patients with acute respiratory failure were intubated, which did not improve with NIPPV.

Significant improvement was observed in clinical and blood gas parameters with NIPPV. The modified Borg's dyspnea score significantly improved with NIPPV at the end of 4, 12 and 24 hours compared with baseline in both type I and type II respiratory failure patients. These findings were supported by a study by Kramer et al. $\frac{3}{2}$ 

Respiratory rate and HR significantly decreased proposing improvement with NIPPV compared with baseline in both type I and type II acute respiratory failure groups at the end of 4, 12 and 24 hours. These findings were in accordance with the studies by Brochard et al. and Agarwal et al. 11,12

In the present study, parameters on arterial blood gas analysis, i.e., pH and PaO<sub>2</sub> improved with NIPPV at the end of 4, 12 and 24 hours in patients with type I respiratory failure compared with baseline. In type II respiratory failure patients, pH, PaO<sub>2</sub> and PaCO<sub>2</sub> improved with NIPPV at the end of 4, 12 and 24 hours compared with baseline. These findings were supported by Ventrella et al. <sup>10</sup> Also, study by Mclaughlin et al. reported that ABG parameters: pH and PaCO<sub>2</sub> were improved at the end of 1 and 4 hours compared with baseline in patients with hypercapnic respiratory failure. <sup>13</sup>

Dryness of mouth and nose was noted as a complication of NIPPV in 3 (6.81%) patients with NIPPV. This may be due to careful selection of patients and interfaces, proper setting of ventilator modalities and close monitoring of patients from the start.

In the present study, the difference between the mean duration of NIV in days, i.e.,  $(3.93 \pm 0.73)$  days for type I and  $(3.6 \pm 1.27)$  days for type II respiratory failure patients were not statistically significant. In contrast, study by Ibrahim et al. reported that the mean duration of NIV was  $(1.92 \pm 1.02)$  days in type I and  $(1.79 \pm 0.9)$  days in type II respiratory failure patients.  $\frac{14}{100}$ 

Also, the difference between the mean duration of length of stay in hospital was not significant in type I (9  $\pm$  1.79) days and type II (8.53  $\pm$  1.69) days respiratory failure patients. The length of hospital stay was (12  $\pm$  4.7) days in the acute hypoxemic respiratory failure in a study reported by Agarwal et al.  $\frac{12}{2}$ 

Rapid reversal of gases, decreased the number of complications and shorter weaning time probably contribute in shortening hospital stay. The shorter duration of hospitalization with the use of NIPPV is cost-effective too.

There are limited previous studies paralleling type I failure and type II failure as a whole. Many studies have compared individual disease groups (e.g., between acute pulmonary edema and acute exacerbation of COPD) or studied a single disease as a whole (e.g., NIV in COPD or NIV in ALI/ARDS) or compared modes of NIV among various types of acute respiratory failure (e.g., CPAP vs BIPAP). The present study aims to standardize the treatment of NIV by using exclusively and only BIPAP and by treating all acute respiratory failure irrespective of the cause and type of respiratory failure. The concept is that no patient presenting with acute respiratory failure be deprived of NIV (if they meet inclusion and exclusion criteria) because of the simple reason that the cause and the type of respiratory failure is unknown.

Factors vital to the success of NIV include careful selection of patients, proper and timed intervention, well-fitting interface, coaching and encouragement of patients, careful monitoring and skilled hospital staff.  $\frac{15}{100}$ 

Outcome predictors are important to identify patients who are less likely to improve with NIV, thus requiring closer observation and readily available means of intubation.

In the present study, comorbidities, such as diabetes mellitus and renal disease were significant in NIV failure group compared with NIV success group. However, comorbidities such as pulmonary hypertension, hypertension, and pulmonary TB were comparable in both groups. Study by Bhattacharyya et al. also reported the comorbidities, such as diabetes mellitus, coronary artery disease, and hypertension associated with NIV failure in patients with hypercapnic respiratory failure. In contrast, Pacilli et al. concluded that

comorbidities significant in NIV failure were dementia, renal disease, obesity, and diaphragmatic paralysis in patients with acute hypercapnic failure. 17 Agreeing to present study, comorbidities, such as diabetes mellitus and renal disease can be considered as predictors of NIV failure.

There was a significant fall in dyspnea score, R and HR at the end of 4 hours compared with baseline in NIV success group but not in NIV failure group. The improvement in pH and PaO2 in NIV success group was statistically significant when compared with NIV failure group.

These findings are in accordance with the study by Bhattacharyya et al., in which there was improvement in heart and RRs, pH and PaCO<sub>2</sub> within the first hour in the success group and these parameters continued to improve even after 4 hours and 24 hours of NIPPV treatment. Also, study by Lin et al. reported that RR improved at the end of 30 minutes with NIPPV and can be considered as predictor of the success of NIV in patients with acute respiratory failure.

According to present study, improvement in dyspnea score, RR, HR, as well as improvement in arterial blood gas parameters, such as pH and PaO<sub>2</sub> within 4 hours of NIPPV could be used to predict the response to NIPPV.

Hence, patients with respiratory failure on NIPPV should be observed about the changes in HR, RR, pH, and PaO<sub>2</sub> at timely intervals, so that patients requiring invasive ventilation may be intubated at the earliest to prevent preventable increase in morbidity and mortality.

### **LIMITATIONS**

- Single center study (the way the NIV service is delivered will depend on the model of hospital care that varies greatly).
- The relatively small sample size and lack of a control group imposed limited value to statistical analysis of group differences between patients with type I respiratory failure and type II respiratory failure. This type of analysis in a small sample sizes may seem inconclusive.
- The placement of an arterial line would have been helped in more frequent ABG assessments.

## CONCLUSION

Study indicates that a trial of BIPAP is effective in improving gas exchange, reducing intubation and length of stay in hospital in patients with acute respiratory failure, suggesting that NIV is a safe and effective means of ventilator support for patients with acute respiratory failure. The study provides strong evidence for the use of NIV (BIPAP) as a first line intervention in patients with acute respiratory failure, irrespective of the type and the cause of acute respiratory failure. However, further studies are required to evaluate other potential predictors of outcome of NIV in acute respiratory failure patients for further improving the success rate of NIPPV.

### **Footnotes**

Source of support: Nil

Conflict of interest: None

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# Figures and Tables

# Table 1

Outcome of noninvasive ventilation

Type of respiratory failure	Success	Failure
Type I $(n = 16)$	14 (87.5%)	2 (12.5%)
Type II $(n = 34)$	30 (88.23%)	4 (11.76%)

**Table 2**Mean vital parameters at different follow-up period in type I and type II respiratory failure patients

Parameter	Time (hour)	Type I	Type II
Respiratory rate	0	$36.38 \pm 4.92$	$33.6 \pm 5.66$
	4	$26.61 \pm 2.98$ **	$26.76 \pm 4.85$ **
	12	$18.15 \pm 3.31$ **	$18.16 \pm 4.02$ **
	24	$16.15 \pm 1.90$ **	$16.76 \pm 3.74$ **
Heart rate	0	$107.23 \pm 1.90$	$102.83 \pm 9.33$
	4	$99.30 \pm 9.74^*$	$96.8 \pm 8.44$ **
	12	$88.76 \pm 6.40$ **	$85 \pm 6.20$ **
	24	$82.76 \pm 4.58$ **	$81.03 \pm 7.56$ **

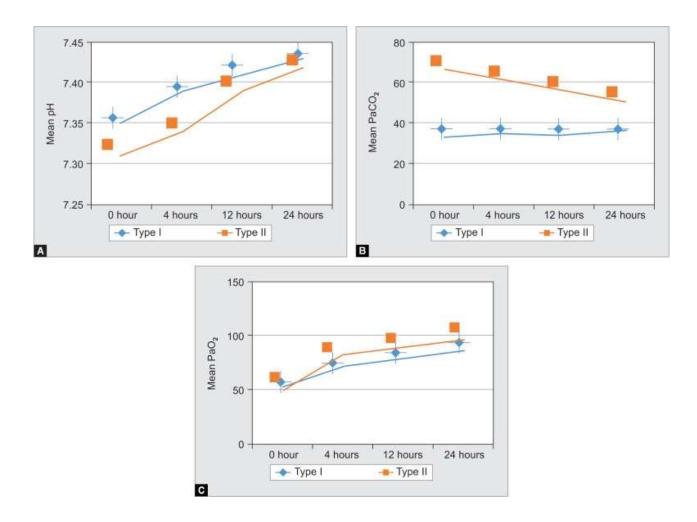
p < 0.01\*\*p < 0.001

**Table 3**Mean change in arterial blood gas parameters at different follow-up period in type I and type II respiratory failure patients

	Time (hours)	Type I	Type II
рН	0	$7.35 \pm 0.04$	$7.31 \pm 0.05$
	4	$7.39 \pm 0.06$ **	$7.34 \pm 0.05$ **
	12	$7.41 \pm 0.05$ **	$7.39 \pm 0.05$ **
	24	$7.43 \pm 0.04$ **	$7.42 \pm 0.04$ **
PaCO <sub>2</sub>	0	$33.56 \pm 6.11$	$66.49 \pm 12.03$
	4	$35.25\pm4.59$	$61.4 \pm 10.04$ **
	12	$33.77 \pm 5.04$	$56.22 \pm 11.15$ **
	24	$36.37\pm6.79$	$51.01 \pm 7.30$ **
PaO <sub>2</sub>	0	$52.69 \pm 4.93$	$50.39 \pm 7.17$
	4	$71.96 \pm 14.63$ **	$82.46 \pm 13.83$ **
	12	$80.43 \pm 14.99$ **	$90.46 \pm 13.98$ **
	24	$86.5 \pm 9.27$ **	$96.0 \pm 13.34$ **

p < 0.01\*\* p < 0.001

Figs 1A to C



Mean change in arterial blood gas parameters at different follow-up period in type I and type II respiratory failure patients

# Table 4

Comparison of mean respiratory rate and mean heart rate at the end of 4 hours from baseline in success and failure and between groups

	Success group $(n = 44)$	Failure group $(n = 6)$
Mean respiratory rate		
0 hour	$34.41 \pm 5.54$	$40.57 \pm 3.40$
4 hours	$26.72 \pm 4.33**$	$37.14 \pm 5.63$
Mean change at 4 hours	$7.72\pm3.73$	$3.42\pm3.59$
p value	0.0068	
Mean heart rate		
0 hour	$104.16 \pm 8.79$	$112.28 \pm 3.14$
4 hours	97.55 ± 8.81 **	$106.57 \pm 4.42^*$
Mean change at 4 hours	$6.60 \pm 6.50$	$5.71 \pm 5.93$
p value	0.7357	

p < 0.05 p < 0.001

Table 5

Comparison of mean ABG parameters at 4 hours from baseline in success and failure and between groups

	Success group $(n = 44)$	Failure group $(n = 6)$
рН		
0 hour	$7.32 \pm 0.05$	$7.30\pm0.027$
4 hours	$7.36 \pm 0.06$ ***	$7.29 \pm 0.02$
Mean change at 4 hours	$0.04\pm0.046$	$0.011 \pm 0.028$
p value	0.0022	
Mean PaCO <sub>2</sub>		
0 hour	$56.63 \pm 18.56$	$58.87 \pm 0.027$
4 hours	$53.49 \pm 14.94$	$55.57 \pm 20.43$
Mean change at 4 hours	$3.04\pm7.34$	$3.3 \pm 13.22$
p value	0.3936, NS	
Mean PaO <sub>2</sub>		
0 hour	$51.09 \pm 6.60$	$50.42 \pm 7.95$
4 hours	$75.13 \pm 15.04$ *	$52.57 \pm 5.96$
Mean change at 4 hours	$24.04 \pm 15.86$	$2.14 \pm 4.81$
p value	0.0013	

<sup>\*</sup>p < 0.001; NS, not significant

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