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Effects of Non-Invasive Ventilation on Cardiac Function in Patients with Acute Respiratory Failure

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ABSTRACT

Background: Non-invasive ventilation (NIV) is widely used to treat chronic obstructive pulmonary disease and heart failure. This study investigated its effects on cardiac function in patients with acute respiratory failure due to COVID-19.
Methods: In this observational cross-sectional study, patients admitted to the ICU of Ayatollah Rouhani Hospital, Babol, who required NIV were evaluated. Heart rate, respiratory rate, arterial blood gas parameters (PaO_2, pH, lactate), and echocardiographic indices, including the left ventricular ejection fraction (LVEF), E, tricuspid annular plane systolic excursion (TAPSE), and inferior vena cava diameter (IVCD), were recorded before and 15 minutes after NIV initiation. Data were analyzed using SPSS.
Results: 34 patients, 15 (44.1%) men and 19 (55.9%) women, were studied. Their average age was 60.4 ± 12.8 years. NIV significantly improved heart rate, respiratory rate, oxygenation, pH, and lactate levels. Echocardiographic parameters E and TAPSE improved significantly, and IVCD increased compared to baseline.
Conclusion: NIV rapidly improves both respiratory and cardiac function in patients with acute respiratory failure due to COVID-19, serving as a potential alternative to invasive ventilation in selected cases.

Introduction

Respiratory failure is defined as the inability of the respiratory system to adequately exchange gases (take in oxygen and simultaneously remove carbon dioxide). As a result, it causes disruption of gas exchange and changes in arterial blood gas values: low PaO_2, high $PaCO_2$, and low pH [1]. Acute respiratory failure can be classified into two types: type 1, or hypoxemic respiratory failure, which is caused by diseases of the lung parenchyma and causes impaired oxygen delivery, and type 2, or hypercapnic respiratory failure, which is caused by muscle failure, hypoventilation, and hypercapnia [1].

The mainstay of management of acute respiratory failure is mechanical ventilation. Mechanical ventilation can be invasive or noninvasive. Respiratory support provided by a face or nasal mask without endotracheal intubation is called noninvasive ventilation (NIV) [2-4]. This approach is indicated in conscious, spontaneously breathing patients. Patients with reversible respiratory failure, such as COPD or cardiogenic pulmonary edema, respond better to noninvasive ventilation. The advantages of noninvasive ventilation include reduced ventilator-associated infection and patient comfort [5-9].

Historically, NIV was first applied in 1990 for the treatment of obstructive sleep apnea using inspiratory positive airway pressure (IPAP) and expiratory positive airway pressure (EPAP) [5]. The low-pressure system improved patient comfort, tolerance, and adherence while

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reducing complications associated with invasive ventilation [6-9]. Over the years, the indications for NIV have expanded to include acute and chronic respiratory diseases due to its ability to correct hypoxia and hypercapnia in spontaneously breathing patients [5-9].

This method is contraindicated in cases such as decreased level of consciousness, lack of respiratory effort, patient uncooperation, increased secretions, unstable hemodynamics, and conditions such as facial trauma [2-3,8-10].

In December 2019, a novel coronavirus was identified as the cause of upper and lower respiratory tract infections in Wuhan, China [11]. A subset of patients with coronavirus develop severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and hypoxic respiratory failure [12]. Some patients with hypoxemia respond to conventional oxygen therapy, such as nasal cannula and mask; however, in severe pulmonary involvement, they may require mechanical ventilation. Noninvasive ventilation is used to delay invasive mechanical ventilation in some patients with COVID-19[12-14].

Invasive ventilation is used in patients who do not respond adequately to drug treatments and non-invasive oxygenation methods and remain hypoxemic [14-15].

Different parameters indicate cardiac function. LVEF is usually used to assess left ventricular systolic function, and the "e prime" and "a prime" waves are used to assess left ventricular diastolic function [16].

In a study by Sanchez et al. in patients with acute respiratory failure with COVID-19 admitted to the intensive care unit (ICU), one of the measures of right ventricular systolic function was tricuspid annular plane systolic excursion (TAPSE) [17].

In spontaneous breathing, the airway and mediastinal pressure are negative during inspiration, so venous return to the right heart is easy, but in non-invasive ventilation, the airway and mediastinal pressure are positive during inspiration, so venous return is difficult. In spontaneous breathing, the left ventricular afterload is high, and systolic blood pressure, which is a sign of ventricular dysfunction, decreases by a maximum of 10 mmHg (relative to expiration) [18].

Hypoxia and hypercarbia have different effects on the systemic and pulmonary vascular function. In addition to the direct effects that it can have on the right and left heart due to increased positive mediastinal pressure, non-invasive ventilation can indirectly improve cardiac function (right and left) by correcting hypoxia and hypercarbia while also not having the complications associated with intubation and invasive ventilation [19]. In Iran, there are no studies that simultaneously examine cardiac function in addition to respiratory function; therefore, the aim of this study is to evaluate the immediate effects of NIV on cardiac function in patients with acute respiratory failure due to COVID-19.

Methods

This observational cross-sectional study (April 2021–April 2022) included 34 ICU patients with acute respiratory failure due to COVID-19 requiring NIV. Inclusion criteria were type 1 (PaO_2 <60 mmHg) or type 2 ($PaCO_2$ > 45 mmHg with pH < 7.35) respiratory failure. Exclusion criteria included airway compromise, hypotension (SBP <90 mmHg), myocardial ischemia, arrhythmia, SpO_2 <75%, agitation, uncooperative patients, and facial trauma or surgery [20].

According to previous studies, the sample size was determined based on the following formula:

$$n \geq \frac{2\left(Z_{1-\alpha/2} + Z_{1-\beta}\right)^2}{\left(\delta_{Difference}/\sigma_{Difference}\right)^2} + \frac{Z^2_{1-\alpha/2}}{2}$$

Sample size was calculated using σ_diff = 5.2 and δ_diff = 3.8 for TAPSE with 5% error and 80% power, requiring at least 32 patients [21].

After selecting patients and placing the orofacial mask, inspiratory and expiratory pressures are adjusted to create an acceptable level of pressure support (PS) (8-12 cm/H2o) and tidal volume (5-7 ml/kg).

In cases of resistant hypercapnia during NIV, the inspiratory pressure level increased, and in cases of hypoxemia, the EPAP values were increased. The oxygen level for all patients was set to FIo2 = 100%. Criteria for failure and discontinuation of NIV (requirement for endotracheal intubation) included the following: failure to correct arterial blood gases (hypoxia and hypercarbia), continued agitation, bradycardia (heart rate <60/min), hypotension (SBP <90 mmHg), respiratory arrest, failure to maintain SpO_2>85%, significant worsening of metabolic or respiratory acidosis (PH <7.20), and mask intolerance [22].

Vital signs (BP, HR, RR), ABG (PaO_2, $PacO_2$, PH, Lactate) and echocardiographic indices (LVEF, E, e', a', TAPSE, IVCD, RV-Sm, and tricuspid regurgitation gradient) were measured before and 15 minutes after noninvasive ventilation. Data were analyzed with SPSS v22; paired t-tests and Pearson correlation assessed changes, with significance set at p<0.05. The study was approved by the Babol University of Medical Sciences Ethics Committee (MUBABOL.HRI.REC.1398.021).

Results

Of 34 patients, 15 (44.1%) were male and 19 (55.9%) were female, with a mean age of 60.4 ± 12.8 years (range 30–89). Baseline characteristics, including BMI and BiPAP indices, are shown in Table 1; vital signs and lab parameters are in Table 2.

Table 3 shows ABG, hemodynamic and respiratory rate parameters in patients before and 15 minutes after NIV. Table 4 shows echocardiographic parameters in patients with acute respiratory failure with COVID-19 before and 15 minutes after noninvasive ventilation.

Paired t-tests indicated significant improvements in heart rate, respiratory rate, SpO_2, PaO_2, pH, and lactate ($p<0.05$). Echocardiographic parameters E and TAPSE increased significantly, and IVCD was higher than baseline, indicating improved cardiac function.

Other variables showed no significant change. The normality of the data was confirmed by the Kolmogorov–Smirnov test. Paired sample T-test analysis indicated that there was a statistically significant difference in HR, respiratory rate, and arterial blood oxygen parameters between before and 15 min after NIV, and the changes in other variables were not statistically significant (P value <0.05).

Table 1- Distribution of height, weight, BMI, and NIV indices

Variable	Amount	Minimum	Maximum
Weight(Kg)	78.9 ± 14.7	54	115
Hight(Cm)	169.6±14.7	151	188
BMI	27.3±4.19	21.7	38.9
PS/Cm/H2O	10.5±1.05	8	12
PEEP/Cm/ H2O	5.32±0.59	5	7

BMI= Body mass index, NIV= Non-Invasive ventilation, PSV= Pressure support, PEEP= Positive end expiratory pressure

Table 2- Distribution of vital signs and laboratory parameters in the first 24 hours of hospitalization

Variables	Amount (Mean ± SD)	Minimum	Maximum
HR/min	90.1±9.43	76	108
MAP/mm/Hg	95.2±11.6	77	125.7
RR/min	31.3±4.72	24	45
Temperature	37.2±0.44	36	38
WBC	9876±4311	4300	21100
HCT (%)	37.3±6.44	26	58
Na(Meq/lit)	136.9±4.55	128	148
K(Meq/lit)	4.14±0.55	2.8	5.1

HR= Heart Rate, MAP= Mean Arterial Pressure, RR= Respiratory Rate, WBC= White Blood Cell, HCT= Hematocrit, Na= Sodiume, K= Potassiume

Table 3- Vital signs of patients before and 15 min after non-invasive ventilation

Vital sign	Amount (Mean ± SD)		Statistic test	P value
	Before NIV	After NIV		
Systolic Blood Pressure(mm/Hg)	129.2 ± 14.7	127.1 ± 17.2	0.952	0.348
Diastolic Blood Pressure(mm/Hg)	78.3 ± 12.3	76.6 ± 11	0.977	0.336
HR/min	90.1 ± 9.43	79.3 ± 9.18	8.406	0.0001
Mean arterial pressure(mm/Hg)	95.2 ± 11.6	93.4 ± 11.7	1.069	0.293
Respiration rate / min	31.2 ± 4.73	25.5 ± 4.57	8.234	0.0001
Arterial blood oxygen(%)	82.2 ± 4.95	90.4 ± 4.14	-10.718	0.0001
PH	7.47 ± 0.07	7.45 ± 0.06	2.883	0.007
$PacO_2$/ mmHg	38.7 ± 8.96	40.1±7.05	-1.285	0.208
HCO3/ mEq/L	26.6 ± 3.85	28.5 ± 12.3	-0.884	0.383
Lactate/ mEq/L	2.07 ± 0.75	1.96 ± 0.76	6.667	0.0001
PaO_2 (mm/Hg)	53.9 ± 5	66.6 ± 8.26	10.-139	0.0001

NIV=Non-Invasive ventilation, HR = heart rate, $PacO_2$ = pressure of arterial CO_2, Pao_2= Pressure of arterial O_2

Table 4- Echocardiographic indices of patients before and 15 minutes after NIV

Echocardiographic parameters	Amount (Mean ± SD)		Statistic test	P value
	Before NIV	After NIV		
EFLV/present	48.6 ± 1.4	49.1 ± 5.23	0.876	0.348
E/cm/sec	70.1 ± 18.7	74 ± 18.5	2.124	0.336
A/cm/sec	70.7 ± 24.6	75.2 ± 27.6	1.08	0.0001
Aprim/cm/sec	10.4 ± 2.74	11.2 ± 3.45	1.652	0.293

Eprim/cm/sec	9.47 ± 3.14	9.5 ± 2.69	0.073	0.0001
RVSM/cm/sec	14.1 ± 1.76	13.7 ± 2.55	-0.951	0.0001
TAPSE/cm	1.79 ± 0.24	1.96 ± 0.35	3.067	0.007
TRG/mmhg	13.5 ± 5.62	13.1 ± 6.49	-0.632	0.208
IVCD/mm	1.57 ± 0.4	1.4 ± 0.	-2.686	0.383

LVEF= Left Ventricular Ejection Fraction, RVSM= Right ventricular systolic tricuspid annulus velocity, TAPSE= Tricuspid annular plane systolic excursion, TRG = tricuspid regurgitation gradient, IVCD= Inferior Vena Cava Diameter

Discussion

In this study, the effects of non-invasive ventilation on cardiac function in patients with acute respiratory failure were investigated.

This study showed that noninvasive ventilation improved cardiac (heart rate, E velocity, TAPSE, and inferior vena cava diameter) and respiratory (respiratory rate, arterial blood oxygen, $PaCO_2$) function in patients with acute respiratory failure with COVID-19 within 15 minutes of NIV initiation.

Similar to our study, many studies have shown that noninvasive ventilation, even before complete correction of hypoxemia or hypercapnia, improves right and left ventricular function due to mechanical effects [23-27].

In the study by Moret et al., the hemodynamic effects of NIV in patients with acute heart failure were evaluated in 20 patients. Data were measured at baseline, 3 hours, and 6 hours after BiPAP. Arterial blood oxygen, pH, $PaCO_2$, lactate HCO_3, tricuspid annular plane systolic excursion, inferior vena cava diameter, and brain natriuretic peptide [BNP] levels were recorded. The results indicated an improvement in these indices over time [23].

Although the results of Moret et al.'s study were similar to ours, a significant difference in our study is the assessment of cardiac function after 15 min of noninvasive ventilation, which can demonstrate the direct mechanical effects of positive mediastinal pressure on the right and left hearts before hypoxia correction. The cardiac effects were after three and six hours, and usually the patient's hypoxia was corrected, and the effects of improving hypoxia on the heart were more pronounced [23].

In the study by Palaiodimos L, obesity (high BMI) was identified as an independent risk factor for mechanical ventilation and death in COVID-19 patients [24].

In the study by KIM et al., 10,861 COVID-19 patients were studied, and the risk of mechanical ventilation in obese patients was 1.89 times that of other patients, which is similar to the present study [25].

Of course, obesity is a risk factor for COVID-19 patients and for acute respiratory failure. Given that FRC is reduced in obese patients, the likelihood of hypoxic acute respiratory failure is higher.

In the study of Jamil et al., non-invasive mechanical ventilation BiPAP was recognized as an essential and safe treatment for patients with severe hypoxia caused by COVID-19 and reduced the hospitalization rate from 18 days in patients with invasive ventilation to 7 days. In the present study, arterial blood oxygen increased from 82.2% before non-invasive ventilation to 90.4% after it, indicating a significant effect of non-invasive ventilation in improving arterial blood oxygen levels, which in turn can be effective in improving the final outcome of COVID-19 patients [26]. The use of PEEP at about 5 cm of water leads to maintaining the minimum tidal volume required for most patients [27].

The effect of invasive ventilation on improving pH has been shown in the study of Dikensoy et al. and also in the study of Ram et al. [28-29]. Improvement in pH is usually due to correction of hypoxia or hypercarbia and better tissue perfusion and reduction of lactate. Also in the present study, the use of non-invasive ventilation led to a significant improvement in lactate levels.

In our study, TAPSE and IVCD increased significantly, suggesting improved right ventricular preload and systolic function. Right ventricular dysfunction is a well-known complication in COVID-19 patients due to increased pulmonary vascular resistance, hypoxia, and systemic inflammation [30-34]. Li et al. and Paternoster et al. studied the cardiac effects of patients with COVID-19. The results of these studies showed impaired right ventricular function in COVID-19 patients, and in the study of Li et al., a decrease in TAPSE was associated with severe COVID-19 disease.

Similar to our study, Li et al. and Paternoster et al. have shown the effect of non-invasive ventilation in improving right ventricular function through improving the TAPSE index in patients with acute respiratory failure with COVID-19 [35-36]. In a study conducted by Zhang Y et al., it was shown that an increase in the E/e′ ratio is seen in patients with a more severe form of COVID-19 disease, and on the other hand, its improvement in non-invasive ventilation that occurred in the present study could indicate the positive effect of this treatment method in improving the prognosis of COVID-19 patients [37].

One of the important points of this study is the investigation of the echocardiographic outcomes of non-invasive ventilation in the first 15 minutes, which alone can show the mechanical effect of this method before the full occurrence of the body's compensatory mechanisms due to the improvement of hypoxia. The limitations of our study include the short follow-up period and the fact that the patients were from a single center. It is recommended that future studies use a larger sample size in a multicenter setting and, if possible, that patients undergo long-term follow-up.

Conclusion

The present study showed that non-invasive ventilation rapidly improves cardiac and respiratory function, including heart rate, respiratory rate, oxygen, arterial blood pH and lactate, E parameter, and TAPSE in patients with acute respiratory failure with COVID-19, and therefore can be used as an alternative to invasive ventilation in these patients.

Abbreviations

ICU: Intensive care units
NIV: Non- invasive ventilation
TAPSE: Tricuspid annular plane systolic excursion
LVEF: left ventricular ejection fraction
PaO_2: Pressure of arterial of O_2
$PaCO_2$: Pressure of arterial of CO_2
IVCD: inferior vena cava diameter

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