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Akut Solunum Yetmezliği Olan Hastalarda Non-invaziv Mekanik Ventilasyon Uygulamasının Perfüzyon İndeksi ve Nabız Basıncı Üzerindeki Etkisi

Effects of Administrating Non-invasive Mechanical Ventilation on Perfusion Index and Pulse Pressure in Patients with Acute Respiratory Failure

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ÖZ

Giriş: Literatürde non-invaziv mekanik ventilasyonun (NIMV) solunum yetmezliği olan hastalarda hipoksemi üzerine etkili olduğu bildirilse de bu uygulamanın hastaların periferik perfüzyonuna etkisi net değildir. Bu çalışmada acil servise başvuran ve NIMV uygulanan hastalarda perfüzyon indeksi ile nabız basıncı arasındaki ilişkinin ve değişimin araştırılması amaçlandı.

Yöntem: Çalışma prospektif ve kesitsel bir araştırma olarak planlanmıştır. İstanbul Eğitim ve Araştırma Hastanesi'nde 2015 yılında iki ay içerisinde NIMV tedavisi görmüş 33 hasta üzerinde yapılmıştır. Perfüzyon indeksi, kan basıncı, kalp hızı, oksijen satürasyonu, NIMV öncesi veya sırasında belirlenen zaman periyotlarında eş zamanlı olarak ölçülerek analiz edildi.

Bulgular: Çalışmaya yaş ortalaması 70,4±8,3 olan toplam 33 hasta alındı. Bu hastaların 15'i (%45,5) erkek, 18'i (%54,5) kadın idi. NIMV uygulanan hastaların oksijen satürasyonunda istatistiksel olarak anlamlı bir artış (p<0,001) ve kalp atım ortalamalarında azalma (p: 0,023) olduğu saptandı. NIMV tedavisi süresince hastaların kan basıncı, nabız basıncı ve perfüzyon indeksinde anlamlı bir değişiklik gözlenmedi (p>0,05).

Sonuç: Akut solunum yetmezliğinde uygulanan NIMV tedavisi hastaların hipoksemisi üzerine olumlu etki gösterirken, hastaların nabız basıncı ve periferik perfüzyonu üzerine olumlu ya da olumsuz bir etkisi bulunmamıştır.

Anahtar Kelimeler: perfüzyon indeksi, non-invaziv mekanik ventilasyon, solunum yetmezliği

ABSTRACT

Objective: S Although it has been reported in the literature that non-invasive mechanical ventilation (NIMV) is effective on hypoxemia in some respiratory failure patients, the effect of this practice on peripheral perfusion of patients is not clear. In this study, the aim is to research changes in and the relation between perfusion index and pulse pressure in patients who have applied to the emergency department and been subject to NIMV.

Method: The study was planned as a prospective and cross-sectional research. It is conducted on 33 patients who have been treated with NIMV within two months in 2015 at Istanbul Training and Research Hospital. Perfusion index, blood pressure, heart rate, oxygen saturation are analysed being simultaneously measured within time periods determined before or during NIMV.

Results: The study includes a total of 33 patients with the average age of 70.4±8.3, consisting of 15 (45.5%) males and 18 (54.5%) females. It is detected that there is an increase in oxygen saturation of the patients who are treated with NIMV (p<0.001) and a decrease in their average of heart rate (p: 0.023), which are statistically significant. There is no significant change has been observed throughout the process of NIMV treatment in patients' blood pressure, pulse pressure and perfusion index (p>0.05).

Conclusion: Whereas NIMV treatment that is applied in acute respiratory failure shows positive effect on patient's hypoxemia, there is no positive or negative effect has been found on patients pulse pressure and peripheral perfusion.

Keywords: perfusion index, non-invasive mechanic ventilation, respiratory failure

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INTRODUCTION

In emergencies, clinicians can gain preliminary insight into patients' hemodynamic status using non-interfering methods, like the perfusion index (PI). This approach proves valuable in emergency medicine practice, particularly concerning perfusion measurement methods that may interfere, as it allows for continuous monitoring and simultaneous measurements. PI is a topic with limited published materials, but large patient samples, especially in emergencies, are urgently needed. Tissues must have adequate perfusion for the prevention of infectious organisms, the maintenance of metabolic processes, and the restoration of tissue (1). The use of non-interfering monitoring methods enables early detection of hemodynamic instability in patients facing short-term emergencies. Studies have demonstrated that addressing hypoxia promptly and ensuring adequate oxygenation can significantly reduce mortality and morbidity (2). A non-interfering monitoring approach is recommended for identifying and rectifying hemodynamic deficits as soon as possible during the initial medical intervention in emergency cases (3). Continuous circulation monitoring assesses peripheral tissue perfusion in clinical settings. This is based on the fact that peripheral tissues exhibit the earliest response to hypoperfusion during shock and the least response to reperfusion during resuscitation. It is crucial to detect circulatory disorders at an early stage (4). A simple clinical assessment, measurements of body temperature, and the use of optical monitoring devices can assist in identifying peripheral circulatory disorders (5-7). The pulse oximetry may reflect peripheral perfusion changes, according to recent research (8). The oxygenation sufficiency of tissues is defined as the balance between the oxygen needed and provided to maintain cellular metabolism and functions at the cellular, tissue, and systemic levels (9). It has not been proven that the intrathoracic pressure generated by non-invasive mechanical ventilation (NIMV) treatment affects patients' vital parameters and perfusion status in any way. This study investigated the effects of NIMV on perfusion index and pulse pressure in patients treated with NIMV in the Emergency Department of a tertiary hospital.

MATERIALS AND METHODS

1. Study Design

The study was designed as a single-center, cross-sectional, and definitive research investigation. Before the commencement of the study, approval was obtained from the Istanbul Training and Research Hospital Ethics Committee (Approval No: 2015/720). The study included all adult patients who sought medical attention at Istanbul Training and Research Hospital between November 1, 2015, and December 31, 2015, and underwent treatment with NIMV.

2. Study Protocol

Both verbal and written consent were obtained from all eligible patients for participation in the study. A patient's consent was obtained directly from them or, in cases where the patient was unable to provide approval, from their accompanying immediate family members (first-degree relatives).

As well as collecting demographic information such as age and gender, pre-NIMV vital signs, including blood pressure, pulse, and oxygen saturation, were also measured. PI measurements were taken simultaneously with vital signs measurements. The non-invasive ventilation (NIV) procedure was performed with a neo-type ventilator (Galileo®, Hamilton Medical AG, Switzerland).

Patients were positioned correctly, and suitable masks were chosen for each patient after providing them with the necessary information. Ventilation was initiated in spontaneous mode with low-pressure settings (inspiration: 10 cmH2O, positive end-expiratory pressure (PEEP): 5 cmH2O, expiration: 5 cmH2O) and limited volume (6-8 mL/kg)." A continuous measurement was conducted over 30 minutes with the PI probe placed on the patient. The blood pressure, heart rate, saturation, and PI values of patients undergoing NIMV were recorded at various intervals. These intervals included before the initiation of NIMV, during NIMV at the fifth, tenth, twentieth, and thirtieth minutes of the treatment, as well as at the fifth minute following the completion of NIMV.

Vital signs of the patients were measured using the General Electric Carescape V100 Dynamap SH612260165SA device. The PI was measured using the saturation probe of the Massimo-SET Root 7362A RDS pulse oximetry device. Non-invasive PI measurements were taken from the fourth distal phalanx of the patient's non-dominant hand, with the hand positioned at the level of the heart. All relevant patient data were meticulously documented during the study.

3. Exclusıon Criteria

The study excluded patients whose cardiopulmonary arrest occurred during the NIMV application, those who needed immediate surgery and advanced treatment, individuals under 18 years old, pregnant women, incompatible patients, and patients whose vital signs could not be measured.

4. Outcome Measures

The primary outcome of the study was the relationship between NIMV and PI. NIMV's effect on pulse pressure was the secondary outcome of the study.

5. Statistical Analysis

The data from the study participants were analyzed using Statistical Package for Social Science (SPSS) 15.0 for Windows. PI data were analyzed for its interrelationship with vital findings of patients treated with NIMV during specified time intervals, including the initial period and the first 30 minutes. Numbers and percentages were given for categorical variables, and averages and standard deviations were given for numerical variables. This study used Student-t Tests when numerical variables and comparisons between independent groups met normal distribution criteria, and Mann Whitney U tests when they didn't. Whenever the differences between dependent group comparisons meet the normal distribution criteria, the study used variance analysis of repetitive measurement, whereas when they do not, Wilcoxon's test was used to compare two groups, whereas Friedman's test was used to compare multiple groups. Wilcoxon tests were used to analyze subgroups, and Bonferroni corrections were applied to the results. The significance level for statistical analysis was set at $p<0.05$.

RESULTS

Initial considerations for the study included 37 patients. Three (12.3%) were excluded due to incompatibility, while one was excluded due to invasive mechanical ventilation. The study included 33 patients, of whom 18 were females (54.5%) and 15 were males (45.5%). It was found that the average age of the patients in the study was 70.4 years±8.3 years (median: 69 years, range: 56-95 years).

Twenty-one patients (63.6%) received NIMV for respiratory failure associated with chronic obstructive pulmonary disease (COPD), and 12 patients (36.4%) received NIMV for acute pulmonary edema. The most common chronic disease among the patients was hypertension (HT). Table 1 presents a distribution of chronic diseases among patients.

Table 1. Recorded Chronic Diseases in NIMV-Treated Patients.

Comorbid chronic disease	Patient Number	Percentage
COPD	18	54,5
CHF	22	66,7
DM	9	27,3
HT	21	63,6
CAD	12	36,4
Asthma	3	9,1
Malignancy	3	9,1
CKD	6	18,2

COPD: Chronic obstructive pulmonary disease, HT: Hypertension
CHF: Congestive heart failure, DM: Diabetes mellitus,
CAD: Coronary artery disease, CKD: Chronic kidney disease,
NIMV: non invasive mechanical ventilation

In patients treated with NIMV due to respiratory insufficiency associated with acute pulmonary edema, no statistically significant changes were observed in systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), heart rate, PI, and pulse pressure averages ($p>0.05$) (Table 2).

SBP, DBP, MAP, heart rate, PI, and pulse pressure averages did not differ statistically significantly among patients treated with NIMV due to respiratory insufficiency associated with COPD ($p>0.05$) (Table 3). Figure 1 illustrates the changes in PI based on the indication for NIMV application.

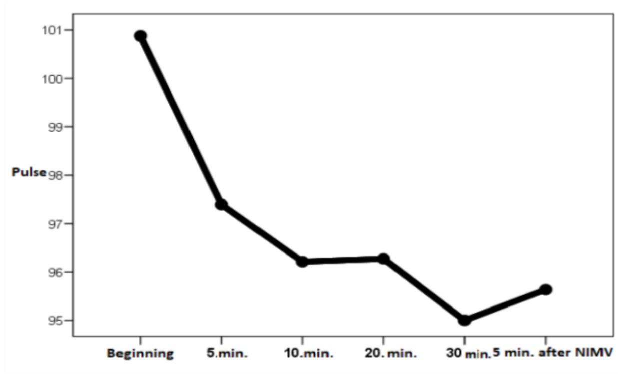

Figure 1. The changes in perfüsion index based on the indication for non-invasive mechanical ventilation application

In terms of the given periods, there was a statistically significant change in oxygen saturation level among patients who were treated with NIMV ($p=0.001$). During monitoring, Oxygen saturation level was statistically significant higher than at the beginning of the study by the thirtieth minute ($p<0.001$). The oxygen saturation level decreased statistically significantly in patients treated with NIMV until the fifth minute following NIMV completion ($p<0.001$). Within the last five minutes, oxygen saturation levels were not statistically different from those at the beginning ($p=0.057$). As shown in Figure 2, oxygen saturation changes in terms of the period set during the application of NIMV.

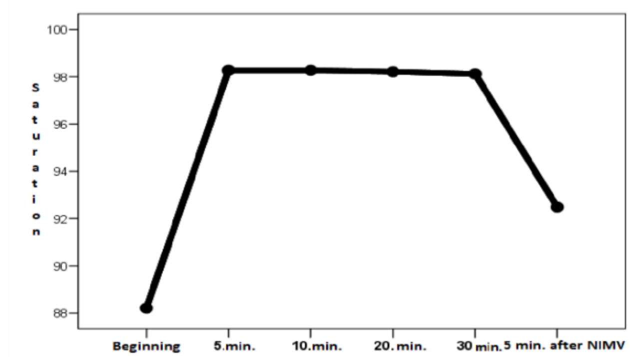

Figure 2. Oxygen saturation changes in terms of the period set during the application of non-invasive mechanical ventilation

Patients undergoing NIMV did not exhibit any statistically significant changes in SBP, DBP, or MAP values throughout the fixed periods ($p=0.065$, $p=0.154$, $p=0.069$, respectively) (Table 4).

The heart rates of NIMV patients changed statistically over the specified periods ($p=0.023$). All monitoring processes showed a statistically significant decrease in patients' heart rates after the fifth minute. Figure 3 illustrates the change in heart rate during the specified periods of NIMV application.

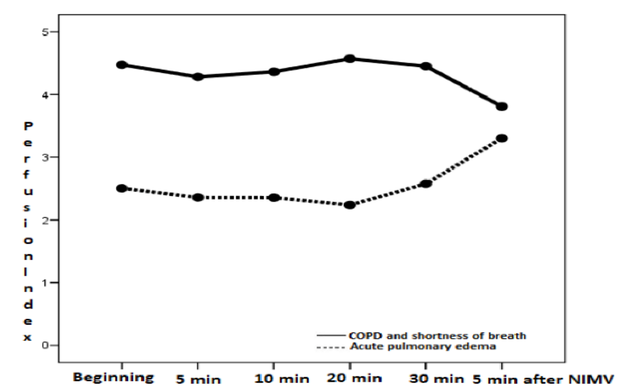

Figure 3. The change in heart rate during the specified periods of non-invasive mechanical ventilation application

In individuals receiving treatment for COPD-related respiratory insufficiency, the average values of SBP, DBP, and MAP were statistically higher than in those receiving treatment for acute pulmonary edema.

Table 2. Changes in Mean Values Of SBP, DBP, MAP, Heart Rate, Oxygen Saturation, PI, Pulse Pressure in NIMV Treated Patients with Acute Pulmonary Edema.

	SBP mean (mmHg) ± SS	DBP mean (mmHg) ± SS	MAP mean (mmHg) ±	Heart rate mean (beats/min) ±	Oxygen saturation mean (beats/min) ± SS	PI mean (beats/min) ± SS	Pulse pressure mean
Before NIMV	179,4 ±34,5	90,2±11,7	119,9±14,5	102,7±24,0	88,3±7,2	2,5±1,9	89,0±34,6
5. minute	162,1±31,6	87,5±18,1	112,4±19,3	101,3±29,9	98,3±2,9	2,4±2,2	74,5±28,3
10.minute	164,3 ±23,0	87,8±11,0	113,3±11,5	99,9±28,7	97,9±2,3	2,4±1,8	75,7±24,1
20.minute	165,1±24,4	87,9±22,0	113,6±17,8	97,5±29,8	98,2±1,9	2,2±2,0	77,2±30,3
30.minute	161,2±21,6	83,2±15,4	107,8±10,3	93,9±27,4	98,0±2,2	2,6±2,9	79,2±29,2
After NIMV 5. minute	157,6±19,6	80,5±10,8	106,2±9,6	95,0±25,4	93,3±3,0	3,3±3,3	77,1±22,6

SBP: Systolic blood pressure, DBP: Diastolic blood pressure, MAP: Mean arterial pressure, PI: Perfusion index, NIMV: Non invasive mechanical ventilation

Table 3. Changes in Mean Values of SBP, DBP, MAP, Heart Rate, Oxygen Saturation, PI, Pulse Pressure in NIMV Treated Because of the Respiratory Insufficiency Comes Along with COPD

	SBP mean (mmHg) ± SS	DBP mean (mmHg) ± SS	MAP mean (mmHg) ± SS	Heart rate mean (beats/min) ± SS	Oxygen saturation mean (beats/min) ± SS	PI mean (beats/min) ± SS	Pulse pressure mean (beat/min) ± SS
Before NIMV	135,5±21,3	72,6±14,7	93,6±15,4	99,9±19,8	88,1±10,3	4,5±5,6	62,3±17,1
5. minute	134,2±26,3	74,2±14,8	94,2±17,2	95,1±19,7	98,3±1,4	4,3±4,5	59,8±18,6
10.minute	132,7±22,2	71,5±12,3	91,9±14,4	94,1±19,6	98,5±1,7	4,4±4,6	59,6±15,2
20.minute	135,0±23,2	74,3±10,1	93,7±13,5	95,6±20,5	98,2±1,8	4,6±4,9	61,2 ±17,5
30.minute	133,2±23,8	71,2±15,1	90,9±15,9	95,6±21,7	98,2±2,2	4,5±5,0	61,1±20,1
After NIMV 5. minute	132,4±22,5	70,8±12,3	91,3±14,3	96,019,9	92,0±6,4	3,8±3,9	60,9±17,0

SBP: Systolic blood pressure,DBP: Diastolic blood pressure,MAP: Mean arterial pressure,PI: Perfusion index, NIMV: Non invasive mechanical ventilation

Table 4. The Changes in Heart Rate, SBP, DBP, MAP in NIMV Treated Patients.

	SBP mean (mmHg) ±SD	DBP mean (mmHg) ±SD	MAP mean (mmHg) ±SD	Heart rate mean (atım/dk) ±SD
Before NIMV	151,5±33,9	79,0±16,0	103,1±19,7	100,9±21,1
5 min	144,4±31,0	79,0±17,1	100,8±19,8	97,4±23,6
10 minutes	144,2±27,0	77,5±14,1	99,7±16,9	96,2±23,0
20 minutes	145,9±27,5	79,3±16,6	100,9±17,8	96,3±23,9
30 minutes	143,4±26,5	75,5±16,0	97,6±16,0	95,0±23,5
5 minutes after NIMV	141,5±24,5	74,3±12,5	96,7±14,6	95,6±21,7
P value	0,065	0,154	0,069	0,023

SBP: Systolic blood pressure,DBP: Diastolic blood pressure,MAP: Mean arterial pressure,NIMV: Non invasive mechanical ventilation

DISCUSSION

The PI calculates and measures the percentage of pulsatile vs. non-pulsatile bloodstream absorption of infrared light (10). As infrared light is absorbed more readily in patients with high peripheral perfusion, a high PI value can be expected. NIMV application promotes positive gas exchange within the lungs. Nevertheless, peripheral perfusion remains unknown as a result of this situation. Within one minute, cardiac output is defined as the amount of blood pumped from the heart ventricle to the peripheral circulation. Heart rate and stroke volume are used to calculate cardiac output. Cardiac output can be affected by a number of factors, including blood volume, systemic vascular resistance, venous compliance, and heart rate.

As a result of the heart's improved pumping strength, cardiac stroke volume increases, directly correlated with the PI in this study. NIMV was performed on mainly COPD patients with respiratory insufficiency. NIMV is most widely used and effective in cases of respiratory failure associated with COPD, according to the literature (11). During the study period, respiratory failure with COPD was prevalent. Patients with acute pulmonary edema who underwent NIMV may be more significantly affected in terms of cardiac output, with a change in the PI, reflecting peripheral perfusion.

Due to its lower inspiration pressure, non-invasive mechanical ventilation (NIMV) is reported to be better tolerated than invasive ventilation (11). According to Colgan et al. (12), NIMV prevents venous return, decreases cardiac output, and may cause systemic hypoperfusion. A non-invasively measured peripheral perfusion was not affected negatively or positively by NIMV application, despite the aim of monitoring potential hypoperfusion following NIMV application.

As a result of continuous positive airway pressure (CPAP) applied with pressures ranging from 3 to 20 cmH2O, Philip-Joet et al observed a decline of 19-23% in cardiac index in healthy individuals. In spite of the study observing a more pronounced decline at CPAP levels exceeding 15 cmH2O, there was no change in average arterial pressure (13). As a result of our study, we did not detect any changes under a 10 cmH2O pressure.

CPAP application with 20 cmH2O was found to reduce cardiac index by 31% in another study by Montner et al (14). Using a nasal mask mitigated this decline. By comparing Philip-Joet et al and Montner et al, it is evident that CPAP applied with 10 cmH2O and CPAP applied with 20 cmH2O have different effects on intrathoracic pressure. There were no hemodynamic effects observed by applying CPAP at pressures between 15-20 cmH2O (13,14). CPAP was applied through both the mouth and nose in our study.

According to other studies, NIMV applied with 3 cmH2O positive end-expiratory pressure (PEEP), in addition to 12 cmH2O CPAP, decreased systemic oxygen presentation and average pulmonary arterial pressure in hypercarbic COPD patients (15).

When applying NIMV through CPAP with an average of 12 cmH2O and oxygen supplementation to patients with acute cardiac insufficiency, Baratz et al observed an increase in cardiac index (16). Increasing inspiration pressure increases intrathoracic pressure, while cardiac output decreases further. The low inspiration pressure applied at 10 cmH2O in our study may explain the lack of a positive or negative relationship between NIMV application and the perfusion index, especially in patients with acute pulmonary edema.

Several studies found that CPAP led to a significant decrease in average heart rate between 9 and 22 beats per minute (bpm) in Kallet et al's review of 41 studies conducted between 1990 and 2008 (17). A similar statistically significant decline in heart rates was observed in our study. Compared to the baseline, this change in heart rate was statistically significant within five minutes of NIMV initiation. Our findings are in line with those of Kallet et al. SBP does not change as a result of NIMV, contrary to the claims of Kallet et al.

Researchers found that when CPAP was applied in the presence of 10 cmH2O pressure to 40 patients with acute pulmonary edema and respiratory insufficiency, there was a statistically significant decrease in SBP of 12±21 mm Hg (18). However, in our study, within the specified periods, there were no statistically significant changes in SBP, DBP, and MAP values. Our study results are consistent with those of other studies that have examined the effects of SBP and MAP on systemic vascular resistance, which is also associated with cardiac output. The perfusion index would have responded similarly if factors affecting cardiac output, such as SBP and MAP, changed significantly.

Additionally, Kallet et al reviewed 20 studies looking at the impact of NIMV on lungs' gas exchange and found positive changes in arterial blood gases in all of them (17). Although no comprehensive assessment of arterial blood gas was made in our study, we observed a statistically significant change in oxygen saturation in patients treated with NIMV over time. The oxygen saturations of patients increased statistically significantly until the thirtieth minute, emphasizing that they were significantly higher at that point in the monitoring process than at the beginning. Our study did not explicitly state that NIMV had led to such improvements.

Pre-NIMV SBP, DBP and MAP values of patients with acute pulmonary edema were higher on average than those of patients with respiratory insufficiency with COPD when the reasons for applying NIMV were taken into account. It is well known that cardiogenic pulmonary edema patients experience compensatory activation of the sympathetic nervous system and neuroendocrine factors (19). This physiological mechanism explains higher average SBP, DBP, and MAP values in cardiogenic pulmonary edema patients.

Among patients with left ventricular systolic dysfunction, pulse pressure is associated with total and cardiovascular mortality as well as recurrent infarction (20). However, there is limited data on the prognostic value of changes in pulse pressure in chronic heart failure patients (HF). Among the first studies to establish the importance of pulse pressure as a prognostic variable, Chae et al suggested that high pulse pressure can predict poor outcomes (21). Stevenson and Perloff demonstrated a close relationship between cardiac index and pulse pressure (22).

In patients with acute cardiogenic pulmonary edema, left ventricular systolic dysfunction activates the adrenergic system, causing peripheral vasoconstriction and increased pulse pressure. In the treatment of cardiogenic pulmonary edema, NIMV has long been used because of its effect on cardiac index and respiratory function (18). A literature review reveals that there aren't many studies investigating pulse pressure and NIMV.

Quintao et al applied CPAP with 6 cmH2O pressure through a nasal mask to 23 patients in a randomized double-blind placebo-controlled study to examine the effect of NIMV on pulse pressure. It was observed that pulse pressure, MAP, and heart rate decreased compared with the control group (19). NIMV caused a significant decline in heart rate in our study, but it did not affect MAP and pulse pressure significantly. CPAP with 6 cmH2O pressure was administered via a nasal mask to patients with stable cardiac insufficiency in Quintao et al's study, which may explain the differences between our study and theirs. As there have been a limited number of studies investigating the effects of NIMV on pulse pressure, it is reasonable to emphasize the need for further research with larger populations.

Limitations

Since we conducted the study in one hospital, the results cannot be generalized. The small sample size of our study was another limitation. To maintain a consistent ventilator mode for all patients, we maintained a consistent setting for the NIMV. Unfortunately, we were unable to assess the PI's effects on different NIMV modes.

Conclusion

It appears that NIMV did not affect the PI, based on our study. Even though the PI was initially used only in anesthetized or critically ill patients, numerous studies have demonstrated its potential to be applied to a variety of diseases. Hypoperfusion can contribute to mortality in many diseases, and considering the widespread use of NIMV, understanding the relationship between NIMV and tissue perfusion is crucial. The PI has been found to act as an early indicator of hypoperfusion in several studies. In order to comprehensively examine the relationship between NIMV and perfusion index, multicenter, large-sample studies are required.

Ethics Committee Approval: Ethical approval was obtained from Istanbul Training and Research Hospital Clinical Research Ethics Committee (06.11.2015 date and 2015- Clinical Trials Ethics Committee-720 number).

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