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## Challenges in Non-Invasive Ventilation: Understanding the Causes of NIV Failure and Complications

Noninvaziv Ventilasyondaki Zorluklar: NIV Başarısızlığı ve Komplikasyonlarının Nedenleri Anlamak

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**Abstract:** Non-invasive ventilation (NIV) has been successfully used in the treatment of acute respiratory failure. The objective of this study was to evaluate complications arising from NIV and their impact on therapy failure, with a specific focus on identifying the most common NIV-related complication leading to NIV failure. A retrospective analysis was conducted on data from 99 patients (54 males, mean age 66 +/- 8 years) who were admitted to Internal Intensive Care Unit between January 1, 2015, and December 30, 2017. These patients received NIV due to acute respiratory failure and were monitored in the intensive care unit for more than 24 hours. The patients' demographic data, causes of acute respiratory failure, and NIV-related complications were obtained from the recorded data. Complications with NIV included discomfort, which developed in 21 patients (21%); air leakage observed in 18 patients (18%), skin erosion in 16 patients (16%), irritated and dry eyes in 9 patients (9%), skin ulcer in 5 patients (5%), abdominal tension in 3 patients (3%), claustrophobia in 2 patients (2%), and hypotension in 1 patient (1%). Univariate and multivariate analyses conducted to evaluate the factors associated with NIV failure showed that discomfort with NIV was the most common factor contributing to failure ( $p = 0.039$ ). Discomfort as an NIV-related complication was identified as the main factor of failure. Choosing the right equipment, providing appropriate ventilatory support, and thorough monitoring are key to minimizing complications and maximizing the effectiveness of NIV therapy.

**Keywords:** Non-Invasive Ventilation, Complications, Discomfort, Treatment Failure

**Özet:** Non-invaziv ventilasyon (NIV), akut solunum yetmezliğinin tedavisinde başarılı bir şekilde kullanılmaktadır. Bu çalışmanın amacı, NIV uygulamasına bağlı gelişen komplikasyonları ve bu komplikasyonların tedavi başarısızlığı üzerindeki etkilerini değerlendirmek olup, özellikle NIV başarısızlığına en sık neden olan komplikasyonu belirlemeye odaklanılmıştır. 1 Ocak 2015 ile 30 Aralık 2017 tarihleri arasında Dahili Yoğun Bakım Ünitesine kabul edilen 99 hastanın (54 erkek, ortalama yaş 66 +/- 8 yıl) verileri üzerine retrospektif bir analiz yapıldı. Bu hastalara, akut solunum yetmezliği nedeniyle NIV uygulandı ve 24 saati aşan süre boyunca yoğun bakım ünitesinde takip edildiler. Hastaların demografik verileri, akut solunum yetmezliği nedenleri ve NIV komplikasyonları kaydedilen verilerden elde edildi. NIV ile ilişkili komplikasyonlar arasında 21 hastada (%21) gelişen rahatsızlık, 18 hastada (%18) hava kaçağı, 16 hastada (%16) cilt erozyonu, 9 hastada (%9) gözlerde iritasyon ve kuruluk, 5 hastada (%5) cilt ülseri, 3 hastada (%3) abdominal gerginlik, 2 hastada (%2) klostrofobi ve 1 hastada (%1) hipotansiyon yer almaktaydı. NIV başarısızlığı ile ilişkili faktörleri değerlendirmek amacıyla yapılan univaryant ve multivaryant analizlerde, NIV kullanımına bağlı rahatsızlık, başarısızlığa en sık katkıda bulunan faktör olarak tespit edilmiştir ( $p = 0,039$ ). Bu çalışmada, NIV ile ilişkili bir komplikasyon olarak rahatsızlık, başarısızlığın ana faktörü olarak belirlenmiştir. Doğru ekipmanın seçilmesi, uygun ventilatuvar desteğin sağlanması ve titiz izlem, komplikasyonların en aza indirilmesi ve NIV tedavisinin etkinliğinin artırılması için önemlidir.

**Anahtar Kelimeler:** Non-İnvaziv Ventilasyon, Komplikasyonlar, Rahatsızlık, Tedavi Başarısızlığı

**Ethics Committee Approval:** This study was designed and conducted in accordance with the ethical guidelines set forth in the Declaration of Helsinki, and the study protocol was approved by the Marmara University Clinical Researches Ethics Committee

(Date: 08.12.2017, Decision No:09.2017.746)

**Informed Consent:** This study did not require informed consent.

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## 1. Introduction

The term non-invasive ventilation (NIV) refers to the application of ventilation without any direct airway access, meaning without the use of an endotracheal or tracheostomy tube[1]. NIV has been used for over 25 years in the treatment of respiratory failure, with its indications continuously expanding and the list of contraindications steadily decreasing [2]. It is widely accepted as an effective treatment for acute respiratory failure, particularly in cases associated with chronic obstructive pulmonary disease (COPD) and acute cardiogenic pulmonary edema[3-6]. Increasingly, more data and efficacy studies are emerging on the use of NIV for other conditions associated with acute respiratory failure. NIV has been shown to reduce the need for intubation, shorten hospital stays, and decrease both morbidity and mortality [7-9].

Successful endpoints are only achieved by appropriate patient selection and tolerance of NIV. The occurrence of pain, pressure sores, agitation, stress, discomfort, or claustrophobia leads to low tolerance and thereby acceptance of NIV [10]. The acceptance of NIV could be related to the patient-device interface and accompanying air leak, the severity of disease condition, agitation, and the mode as well as settings of NIV being used.

NIV failure, defined as the need for endotracheal intubation, the failure rate of NIV varies from 5% to 40% [8, 11, 12]. Studies have identified several factors influencing failure, patient discomfort or rejection[10, 13, 14] including the underlying disease [14, 15], baseline arterial blood gas values and severity of the condition [16], the experience of the team administering NIV, and the equipment used [17].

NIV is generally a safe treatment method, with most complications being minor and related to the mask. Major complications are rare [18].

The number of studies comparing the impact of complications arising during NIV on the failure is limited. The objective of this retrospective cross-sectional study was to determine the complications in subjects who underwent NIV in our center and evaluate the impact of complications on the failure of NIV.

## 2. Materials and Methods

This was a retrospective cross-sectional study conducted between January 2015 and December 2017. We retrospectively included subjects aged 18

years or older who were admitted to our 12-bed internal intensive care unit (ICU) with acute respiratory failure and underwent NIV. Since this was a retrospective analysis based on patient records, informed consent was not required. The study protocol was approved by the institutional ethics committee (Approval date: 20.09.2017, No: 746).

NIV was initiated in accordance with the clinical protocols of the ICU at that time, for patients who met one or more of the following criteria: hypercapnia ( $\text{PaCO}_2 > 45$  mm Hg) with  $\text{pH} < 7.35$ , hypoxemia ( $\text{PaO}_2/\text{FiO}_2 < 200$ ), respiratory rate  $> 25/\text{min}$  despite normal blood gas parameters, or use of accessory respiratory muscles.

NIV failure was defined by the need for endotracheal intubation [12]. Indications for emergency intubation included respiratory or cardiac arrest, unconsciousness, agitation unresponsive to sedation, massive aspiration, inability to clear secretions, heart rate  $< 50$  with impaired consciousness, or hemodynamic instability unresponsive to fluids and vasoactive agents [19].

Patients were intubated due to NIV failure if they exhibited one or more of the following: an increase in  $\text{PaCO}_2 \geq 10$  mm Hg and a decrease in  $\text{pH} \geq 0.10$ ;  $\text{PaO}_2 < 60$  mm Hg or  $\text{SaO}_2 < 90\%$  despite high  $\text{FiO}_2$ ; tachypnea, use of accessory respiratory muscles, thoracoabdominal paradox, inability to protect the airway, excessive pulmonary secretions, or altered mental status[20, 21] Conventional intensive care ventilators were used throughout the study period.

In this retrospective study, according to the clinical protocol, NIV had been interrupted every 4 hours for facial and oral care. Arterial blood gases had been measured 1 hour after the initiation of NIV and then twice daily or when clinically indicated. Respiratory patterns, consciousness, and vital signs had been continuously monitored throughout the treatment.

The selection of oronasal or full-face masks (Respironics, Inc.) was made based on clinical practices in place during the study period. An appropriately sized mask was chosen based on the patient's facial type. However, records on the number of patients and the type of interface used were not available. Initial NIV settings included an inspiratory pressure of 10 cm  $\text{H}_2\text{O}$  and an end-expiratory pressure of 5 cm  $\text{H}_2\text{O}$ , which was adjusted to achieve a tidal volume of at least 5 ml/kg

and a respiratory rate below 25/min.  $\text{FiO}_2$  was titrated to maintain an oxygen saturation of at least 90%. Subjects who had been receiving bronchodilator therapy continued to do so via nebulization. Oral feeding was permitted after the first 24 hours unless contraindicated.

Demographic data, causes of acute respiratory failure, arterial blood gas tensions at the initiation of NIV and NIV-related complications were collected from the patients' medical records. Based on the outcomes and records, complications of non-invasive ventilation (NIV) were categorized under the following groups: discomfort, skin erosion, air leakage, hypotension, skin ulceration, eye irritation, abdominal distension, and claustrophobia.

Discomfort in NIV refers to the physical and psychological strain caused by factors such as mask type, strap tightness, and airflow pressure, often reducing patient tolerance and potentially leading to NIV failure [22].

### Statistical Analysis

SPSS 21.0 Statistics Software Program was used for analysis of the study results. We used Pearson Chi-square test and Fisher's exact tests and Mann-Whitney U Tests for univariate analysis of risk factors. A multivariate logistic regression analysis was used to assess the significant factors from univariate analysis. Pearson Chi-square test and risk analysis were carried out to evaluate the relationship between mortality and achievement. The results

were evaluated at a confidence interval of 95% and a significance level of  $p < 0.05$ .

### 3. Results

Nearly 500 patients were admitted to the ICU over the two-year period. Of these, the study included a total of 99 subjects who were admitted with respiratory failure from various causes and received NIV. The demographic characteristics of 99 subjects are shown in (Table 1).

NIV was administered to 52 patients (52%) for COPD, 13 patients (13%) for acute pulmonary edema associated with congestive heart failure, 25 patients (25%) for pneumonia, and 9 patients (9%) for other reasons.

NIV failure was observed in 25 patients (25%). Discomfort related to NIV developed in 21 patients (21%), while air leaks were documented in 18 patients (18%), skin erosion in 16 patients (16%), irritated and dry eyes in 9 patients (9%), skin ulcers in 5 patients (5%), abdominal tension in 4 patients (4%), and claustrophobia in 2 patients (2%). (Table 2).

The univariate and multivariate analyses showed that discomfort to NIV was significantly effective in the failure of NIV ( $p=0.039$ ) (Table 2 and Table 3). Furthermore, while all subjects successfully treated with NIV were discharged from the hospital, the mortality rate was 64% among those who failed NIV (Table 4). Of the 99 patients who received NIV, 83 were discharged.

**Table 1.** Demographic characteristics and indications for the use of NIV in patients

Patients	
Sex (Female/Male) (n)	45/54
Age (year)	66+/-8
Exacerbation in COPD (n)	52
Pneumonia (n)	25
Acute Cardiogenic Pulmonary Edema (n)	13
Obesity Hypoventilation Syndrome (OHS) (n)	4
Neuromuscular Diseases (n)	3
Asthma (n)	2

**Table 2.** Complications Associated with Failure and Success (Univariate Chi-square analysis)

		Failure		Success		p
		n	%	n	%	
Presence of complications	No	11	24,4%	34	75,6%	$X^2=0,029$ $p=0,527$
	Yes	14	25,9%	40	74,1%	
Discomfort	No	16	20,5%	62	79,5%	$X^2=4,376$ $p=0,039$
	Yes	9	42,9%	12	57,1%	
Skin Erosion	No	22	26,5%	61	73,5%	$X^2=0,428$ $p=0,380$
	Yes	3	18,8%	13	81,2%	
Air Leakage	No	22	27,5%	59	72,5%	$X^2=0,908$ $p=0,264$
	Yes	3	16,7%	15	83,3%	
Hypotension	No	24	24,5%	74	75,5%	$X^2=2,990$ $p=0,253$
	Yes	1	100,0%	0	0,0%	
Skin Ulcer	No	24	25,5%	70	74,5%	$X^2=0,077$ $p=0,627$
	Yes	1	20,0%	4	80,0%	
Eye irritation	No	23	25,6%	67	74,4%	$X^2=0,048$ $p=0,593$
	Yes	2	22,2%	7	77,8%	
Abdominal distension	No	24	25,3%	71	74,7%	$X^2=0,000$ $p=0,736$
	Yes	1	25,0%	3	75,0%	
Claustrophobia	No	24	24,7%	73	75,3%	$X^2=0,662$ $p=0,443$
	Yes	1	50,0%	1	50,0%	

**Table 3.** Factors Associated with Failure (Multivariate Logistic Regression Analysis)

	B	p	OR	95% C.I. for OR	
				Lower	Upper
Hypoxemic Respiratory Failure	-1,531	0,008	4,62	1,50	14,25
Discomfort	-2,062	0,002	141,52	2,07	29,91
Constant – model constant	2,094	0,000	8,12		

**Table 4.** Relationship Between Mortality and Failure

(Chi-Square and Risk Analysis)

		Discharged		Ex		p
		n	%	n	%	
Failed	Failed	9	36,0%	16	64,0%	$X^2=56,490$ $p=0,000$
	Successfully treated	74	100,0%	0	0,0%	

#### 4. Discussion

Our study demonstrated that discomfort related to NIV, along with other complications such as air leaks, skin erosion, and claustrophobia, was a significant factor contributing to the failure of non-invasive ventilation. This finding provides valuable insights into the critical role that patient tolerance and the management of NIV-related side effects play in determining the success of NIV treatment. Additionally, the study underscores the significant difference in outcomes, with a high mortality rate among patients who experienced NIV failure, highlighting the importance of developing better strategies to improve patient comfort with NIV therapy.

NIV failure is influenced by several factors, including delayed initiation of NIV, inappropriate ventilation pressures, limited experience of the clinical team, and, most importantly, the patient's clinical condition.

In our study all patients who were successfully treated with NIV were discharged from the hospital, while those who experienced NIV failure had an ICU mortality rate of 64%, consistent with findings from the study by Demoule et al.[23].

Although NIV is generally considered more comfortable for patients than invasive mechanical ventilation (IMV), discomfort can affect as many as 30–50% of patients. Despite the best efforts of skilled caregivers, discomfort remains a contributing factor in 12-33% of NIV failures [24-26]. In our study, discomfort related to NIV was observed in 21 patients (21%).

Discomfort during NIV is often related to the device and the ventilation modality used [24]. Among various types of NIV masks, tolerance is lowest for the mouthpiece, followed by nasal and oronasal masks [27]. All attachment systems are considered to cause varying levels of discomfort on the skin, and tightening the straps to reduce air leaks and improve patient-ventilator synchrony can further decrease tolerance [27]. In some cases, switching to a different strap system or mask may be necessary to alleviate discomfort [28]. Helmets tend to be better tolerated than masks, leading to longer usage and a lower NIV failure rate [29]. However, some studies have reported similar comfort levels between the two interfaces or even greater discomfort with the helmet [30].

Discomfort has been identified as a key factor in failed NIV application [31]. Exploring solutions to reduce discomfort may enhance the success of this treatment method.

Air leakage from the mask was identified as one of the factors leading to failure in a multi-center prospective study by Carlucci et al.[10]. In our study, air leakage from the mask was observed in 18% of the patients. Other studies have reported air leak rates as high as 50% [28, 32]. The lower incidence of air leakage in our study may be attributed to the careful selection of the most appropriate masks before initiating NIV.

In selected patients, and when clinical status allows, a trial of high-flow nasal cannula (HFNC) oxygen therapy can be considered as an alternative in cases of intolerance to the various interfaces used for NIV [33].

The ventilator machine is obviously important during NIV. Consistent with recent findings [34], asynchrony events are significantly reduced when using a dedicated NIV ventilator compared to ICU ventilators with an NIV algorithm. This is likely due to the dedicated ventilator's more efficient and specialized system for compensating air leaks [35]. Various strategies can help reduce discomfort during NIV, including the use of ventilators with air-leak detection and compensation algorithms, implementing leak-insensitive ventilation modes, lowering the applied pressure, and selecting the appropriate interface [36].

Moreover, even though sedation is not mandatory during NIV therapy, the addition of a small amount of analgosedation like dexmedetomidine may help selected patients to better tolerate NIV, which can help to achieve the desired outcomes. A systematic review found that using sedative and analgesic drugs, particularly dexmedetomidine, during NIV can enhance clinical outcomes in patients with acute respiratory failure. Dexmedetomidine was shown to be superior to other sedatives in improving certain clinical parameters and increasing patient compliance with NIV. However, it is essential to closely monitor patients' vital signs to ensure the safe administration of these drugs and optimize the effectiveness of NIV therapy [37].

In a retrospective study on patients who received NIV after extubation and had discomfort to NIV interface in seven intensive care units (ICUs),



sedation and/or analgesia were used in 41 out of 80 patients (analgesia in 17, sedation in 11, and both in 13) at some time during NIV therapy. Those who received sedation and/or analgesia showed reduced NIV failure rate (15 vs 38%,  $p = 0.015$ ), mortality (7 vs 33%,  $p = 0.004$ ), and length of ICU stay after extubation [38]. In our study, no sedative agents were used in patients undergoing NIV. The high rate of NIV failure due to discomfort observed in our study may be one of the contributing factors.

To date, there are no principles or algorithms to guide the use of sedation during NIV [39]. Observational studies and clinical trials have explored the potential use of sedatives or analgesics to alleviate patient discomfort and address or prevent NIV intolerance. However, there is insufficient strong evidence to establish a standardized guideline, and the selection of drugs is largely guided by the physician's clinical judgment and preference. [40].

Our study has two primary limitations. Firstly, it was a single-center study, and secondly, data collection was restricted to patient records.

## 5. Conclusion

In conclusion, to achieve the best patient outcomes, NIV should be administered by a skilled and experienced team. Proper patient selection, guided by clinical judgement and existing protocols, is crucial, especially when considering factors that increase the risk of NIV failure. Continuous monitoring is essential, particularly in an ICU or step-down unit, until the patient is stabilized. This should include not only tracking vital signs and gas exchange but also ensuring patient comfort, managing air leaks, and optimizing patient-ventilator interaction. Choosing the right equipment, providing appropriate ventilatory support, and thorough monitoring are key to minimizing complications and maximizing the effectiveness of NIV therapy

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