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Research Article

Factor for predicting non-invasive ventilation failure in very old patients with hypoxemic respiratory failure in intensive care unit

Yoğun bakım ünitesinde hipoksemik solunum yetmezliği olan çok yaşlı hastalarda noninvaziv ventilasyon başarısızlığını tahmin eden faktörler

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Abstract

Aim: This study aimed to investigate the efficacy of NIV in patients with pneumonia-associated acute hypoxemic respiratory failure (AHRF) and to identify factors that predict NIV failure.

Material and Methods: A total of 50 very elderly patients (aged 85 and older) with pneumonia-associated AHRF were retrospectively evaluated from January 2022 to August 2022. Failure of NIV was defined was characterized by a transition to mechanical ventilation (either through tracheal intubation or tracheostomy), discharge under "hopeless" conditions while still on NIV, or death during NIV.

Results: The mean age of the patients was 87.4±2.4 years, median SOFA score was 5, median duration of NIV was 4 days, and median length of stay in the ICU for the patients was 7 days. It was determined that 48% of the patients experienced NIV failure due to worsening clinical conditions. The SOFA score, levels of procalcitonin, CRP, heart rate, and respiratory rate were higher in the NIV failure group compared to the NIV successful group. An increased SOFA score (OR= 1.51, 95% CI= 1.11-2.06, p= 0.009), elevated CRP levels (OR= 1.03, 95% CI= 1.01-1.05, p= 0.003), and increased respiratory rate (OR= 1.18, 95% CI= 1.01-1.38, p= 0.039) were identified as independent predictors of NIV failure.

Conclusion: In very elderly patients with AHRF due to pneumonia, the use of NIV may offer a significant survival benefit if patients are closely monitored and potential risk factors such as systemic inflammation parameters, SOFA score, and respiratory rate are considered.

Keywords: Critical illness, elderly, noninvasive ventilation, pneumonia, respiratory failure

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Öz

Amaç: Bu çalışma, pnömoniye bağlı akut hipoksemik solunum yetmezliği (AHRF) olan hastalarda NIV'in etkinliğini araştırmayı ve NIV başarısızlığını öngören faktörleri belirlemeyi amaçladı.

Gereç ve Yöntemler: Ocak 2022 ile Ağustos 2022 tarihleri arasında pnömoniye bağlı AHRF olan toplam 50 çok yaşlı hasta (85 yaş ve üzeri) retrospektif olarak değerlendirildi. NIV başarısızlığı, mekanik ventilasyona geçiş (ya trakeal entübasyon ya da trakeostomi yoluyla), NIV kullanımı sırasında "ümitsiz" durumlarda taburcu edilme veya NIV sırasında ölüm ile tanımlandı.

Bulgular: Hastaların ortalama yaşı 87,4±2,4 yıl, medyan SOFA skoru 5, medyan NIV süresi 4 gün ve hastaların yoğun bakımda kalış süresi medyan 7 gün olarak belirlendi. Hastaların %48'inde kötüleşen klinik durumlar nedeniyle NIV başarısızlığı yaşandığı belirlendi. SOFA skoru, prokalsitonin seviyeleri, CRP, kalp hızı ve solunum hızı, NIV başarısızlığı yaşayan grupta NIV başarılı olan gruba göre daha yüksekti. Artmış SOFA skoru (OR= 1,51, %95 CI= 1,11-2,06, p= 0,009), yükselmiş CRP seviyeleri (OR= 1,03, %95 CI= 1,01-1,05, p= 0,003) ve artmış solunum hızı (OR= 1,18, %95 CI= 1,01-1,38, p= 0,039) bağımsız NIV başarısızlık öngörücüleri olarak tanımlandı.

Sonuçlar: Pnömoniye bağlı AHRF olan çok yaşlı hastalarda, NIV kullanımı, hastalar yakından izlendiği ve potansiyel risk faktörleri dikkate alındığı takdirde önemli bir sağkalım avantajı sağlayabilir. Bu kohortta NIV başarısızlığını öngörmek için sistemik inflamasyon parametreleri, SOFA skoru ve solunum hızı kullanılabilir.

Anahtar Kelimeler: Kritik hastalık, ileri yaş, noninvaziv ventilasyon, pnömoni, solunum yetmezliği

Introduction

Noninvasive ventilation (NIV) provides respiratory support through either a nasal mask, a full-face mask, or a helmet masks, unlike tracheal intubation or tracheostomy, does not bypass the upper airway [1]. NIV offers significant benefits over invasive methods, such as preventing complications from endotracheal intubation, minimizing patient discomfort, and preserving airway protective mechanisms [2, 3].

Acute hypoxemic respiratory failure (AHRF) is a common reason for admission to intensive care units (ICUs) and is a significant problem that leads to endotracheal intubation and invasive mechanical ventilation [4]. On the other hand, more than half of the patients admitted to ICUs are affected by hypoxemia [5]. The use of NIV for AHRF remains a contentious issue. Due to a lack of conclusive evidence, the European Respiratory Society/ American Thoracic Society's guideline for acute respiratory failure has not made a recommendation regarding the use of NIV in de-novo AHRF [6]. Results from a meta-analysis indicates that using NIV in AHRF decreases the need for endotracheal intubation and lowers hospital mortality [7]. However, there is concern about the possibility of NIV failure and the resulting increased mortality from delayed intubation in elderly patients, especially cases with pneumonia [8, 9]. In addition, NIV is often recommended for respiratory support in patients with a do-not-intubate (DNI) order [10, 11].

Identifying the factors of NIV failure in elderly patients with pneumonia-associated acute respiratory failure can enable safe usage of NIV or indicate the necessity for early intubation [12]. However, in this cohort, particularly in very old cases, there is limited research evaluating the factors contributing to NIV failure. Therefore, this study aimed to investigate the efficacy of NIV in patients with pneumonia-associated AHRF and to identify factors that predict NIV failure.

Material and Methods

This retrospective study was conducted on elderly patients with respiratory failure in the ICU of Internal Medicine of University of Health Sciences Konya City Hospital between January 2022 to August 2022. This study was approved by the Ethics Committee for Non-Drug and Non-Medical Device Research at Konya Trade Chamber Karatay University Faculty of Medicine (Date: 21.09.2022, Decision No: 2022/042) and was carried out in accordance with the relevant ethical guidelines and the Helsinki Declaration (2013 Brazil revision). The need for informed consent was waived under the approval of the Ethics Committee due to the retrospective design.

In previous studies conducted on elderly and very elderly patients, the failure rate of NIV was reported to be approximately 40% [12, 13]. Accordingly, the sample size was calculated to be at least 41 patients using the formula n = [Z2 × P × (1 - P)] / d2 with a 90% confidence interval. Here, the Z value was taken as 1.96, the p value as 0.40, and the precision (d) value as 0.15.

Study population

We retrospectively evaluated a total of 85 elderly patients who received NIV for respiratory failure in the ICU of internal medicine. The inclusion criteria were patients aged 85 years and older, having pneumonia-associated AHRF, and complete patient data. Patients under the age of 85, those with respiratory failure due to causes other than pneumonia, hypercapnic respiratory failure, use of NIV for palliative care, use of NIV despite contraindications such as myocardial infarction or cardiac arrest, use of NIV for acute postoperative respiratory failure, NIV weaning, and those with missing clinical data were not included in the study. Following the exclusion process, 50 very elderly patients (aged 85 and older) with pneumonia-associated respiratory failure were enrolled in this study.

Collection of Data

The clinical demographic findings, laboratory findings, and imaging methods of the study population were obtained from the electronic files of the patients. The ratio of partial pressure of oxygen (PaO2) to fraction of inspired oxygen (FiO2) and partial pressure of carbon dioxide (PCO2) was determined using the initial arterial blood gas analysis conducted by ABL90 FLEX PLUS device (Radiometer, Copenaghen, Denmark) in the ICU department. The complete blood counts of all of the patients were measured at admission of ICU department. Patients' venous blood samples were evaluated using a Roche Cobas 8000 device (Roche Diagnostics, Mannheim, Germany). Levels of hemoglobin were determined photometrically, platelet count via the impedance method, C-reactive protein (CRP) using the immunoturbidimetric method, albumin through the bromocresol green method, and creatinine with the kinetic colorimetric Jaffe method.

Definitions

AHRF was defined as having an arterial PaO2 to FiO2 ratio of 300 or less, accompanied by a normal or low arterial PaCO2 [14]. The diagnosis of pneumonia was established through typical symptoms like fever and cough, increased inflammatory markers, and the presence of pneumonic consolidation on chest X-rays. Mortality referred to any death that took place from the time of admission to the time of discharge from the ICU. The success of NIV was defined by the patient's ability to be weaned off the device successfully and subsequently discontinue its use. Failure of NIV was defined was characterized by a transition to mechanical ventilation (either through tracheal intubation or tracheostomy), discharge under "hopeless" conditions while still on NIV, or death during NIV.

Statistical analysis

All data were analyzed with IBM SPSS Statistics for Windows 20.0 (IBM Corp., Armonk, NY, USA). Numerical data determined to be normally distributed based on the results of Kolmogorov-Smirnov tests are given as mean ± standard deviation (SD) values while non-normally distributed variables are given as median (25th-75th quartile) values. For comparisons between groups, Student T-test and Mann-Whitney U test were used in line with the normality of the considered distribution. Categorical variables are given as numbers and percentages, and inter-group comparisons were conducted with Chi-square and Fisher exact tests. Significance was accepted at $P < 0.05$ (*) for all statistical analyses

Results

The study included 50 patients, comprising 25 men and 25 women, with an average age of 87.4 ± 2.4 years (range = 85 – 97 years). Among the patients, 60% suffered from hypertension (n = 30), 58% from heart failure (n = 29), 52% from kidney disease (n = 26), and 42% from diabetes mellitus (n = 21). The median SOFA score was 5 (range = 2 – 11) (Table 1). It was found that an oronasal mask was used in all patients. The initial NIV setting was in pressure support mode and EPAP settings were 6.1 ± 0.8 cm H2O. It was also observed that during NIV, no patients required sedatives and there were no complications. The median duration of NIV was 4 days (range = 3 – 8 days) and median length of stay in the ICU for the patients was 7 days (range = 5 – 25 days). It was determined that 48% (n = 24) of the patients experienced NIV failure due to worsening clinical conditions. These patients were intubated and received mechanical ventilation, but it was later established that they died in the following days. In this context, the NIV failure rate was 48% (n = 24). The patients' demographic and clinical characteristics are detailed in Table 1 and 2.

Demographic characteristics did not show significant differences between the successful and failure NIV groups. The median SOFA score (7 vs. 5, $p = 0.028$), median procalcitonin level (0.9 vs. 0.3 µg/L, $p = 0.027$), and median CRP level (90.5 vs. 66.0 mg/dL, $p = 0.004$) were higher in the NIV failure group compared to the NIV successful group. Other laboratory findings did not show significant differences between the groups (Table 1).

The mean heart rate (110.9 ± 11.3 vs. 95.4 ± 13.2 beats/min, $p < 0.001$), and mean respiratory rate (24.8 ± 1.9 vs. 18.6 ± 1.9 breaths/min, $p < 0.001$) were higher in the NIV failure group compared to the NIV successful group, while the mean systolic blood pressure (81.7 ± 12.2 vs. 110.1 ± 12.6 mmHg, $p < 0.001$) was lower. The mean EPAP (6.7 ± 0.6 vs. 5.7 ± 0.7 cm H2O, $p < 0.001$) was higher in the NIV failure group compared to the NIV successful group. Other clinical findings did not show significant differences between the groups (Table 2).

Potential factors associated with NIV failure were included in a multivariable regression model. Accordingly, an increased SOFA score, elevated CRP levels, and increased respiratory rate were identified as independent predictors of NIV failure (Table 3).

Table 1. Demographic and laboratory findings of patients.

Variables	All population n = 50	Noninvasive ventilation		p-value
		Success n = 26	Failure n = 24	
Age, years	87.4 ± 2.4	87.5 ± 2.5	87.2 ± 2.2	0.627
Gender, n (%)				
Female	25 (50.0)	14 (53.8)	11 (45.8)	0.778
Male	25 (50.0)	12 (46.2)	13 (54.2)	
Comorbidity, n (%)				
Hypertension	30 (60.0)	16 (61.5)	14 (58.3)	0.995
Heart failure	29 (58.0)	13 (50.0)	16 (66.7)	0.265
Kidney disease	26 (52.0)	15 (57.7)	11 (45.8)	0.572
Diabetes mellitus	21 (42.0)	11 (42.3)	10 (41.7)	0.999
SOFA score	6 (3-8)	5 (3-7)	7 (5-9)	0.028*
Laboratory parameters				
Neutrophils, $\times 10^3$ µ/L	8.1 (6.7-11.6)	7.8 (5.8-11.3)	9.6 (7.7-12.5)	0.159
Lymphocytes, $\times 10^3$ µ/L	2.3 (1.9-3.3)	2.4 (2-3.6)	2.0 (1.7-2.7)	0.125
Platelets, $\times 10^3$ µ/L	183 (156-231)	174 (152-232)	193 (167-221)	0.393
Lactate, mmol/L	2.0 ± 0.5	2.0 ± 0.6	1.9 ± 0.3	0.821
Creatinine, mg/dL	1.5 ± 0.7	1.7 ± 0.7	1.4 ± 0.7	0.192
Procalcitonin, µg/L	0.8 (0.3-1.5)	0.3 (0.2-1.4)	0.9 (0.6-1.7)	0.027*
CRP, mg/dL	87.5 (65.0-112.4)	66.0 (53.0-104.5)	90.5 (83.0-129.5)	0.004*
Albumin, mg/dL	2.9 ± 0.4	2.9 ± 0.4	2.7 ± 0.4	0.083

The data are expressed as the mean ± SD or median (IQR) or number (%). Abbreviations: CRP, C-reactive protein; SOFA, sequential organ failure assessment.

Table 2. Clinical findings of the patients.

Variables	All population n = 50	Noninvasive Ventilation		p-value
		Success n = 26	Failure n = 24	
Physiologic parameters				
Systolic BP, mmHg	96.4 ± 18.9	110.1 ± 12.6	81.7 ± 12.2	<0.001*
Heart rate, beats/min	102.8 ± 14.5	95.4 ± 13.2	110.9 ± 11.3	<0.001*
Respiratory rate, breaths/min	21.6 ± 3.7	18.6 ± 1.9	24.8 ± 1.9	<0.001*
Arterial pH	7.3 ± 0.1	7.3 ± 0.1	7.3 ± 0.1	0.375
PaO2/FiO2 ratio	210.9 ± 34.5	218.8 ± 34.9	201.8 ± 34.6	0.088
PaCO2, mmHg	38.8 ± 3.9	38.4 ± 3.8	38.8 ± 3.8	0.695
Interface type, n (%)				
Oronasal	55 (100)	26 (100)	24 (100)	-
Initial mode, n (%)				
Pressure support mode	55 (100)	26 (100)	24 (100)	-
Initial setting				
EPAP, cm H2O	6.1 ± 0.8	5.7 ± 0.7	6.7 ± 0.6	<0.001*
Tidal volume, mL	442.0 ± 24.4	446.0 ± 15.7	436.8 ± 21.9	0.092
Duration of NIV, days	4 (3-5)	4.5 (3-5)	4 (3-5)	0.621
Duration of ICU stay, days	7 (6-8)	7 (6-8)	6 (6-7.5)	0.251
Duration of hospital stay, days	14 (13-17)	15 (13-17)	14 (12.5-16)	0.323

The data are expressed as the mean ± SD or median (IQR) or number (%). Abbreviations: BP, blood pressure; EPAP, expiratory positive airway pressure; FiO2, fraction of inspired oxygen; ICU, intensive care unit; NIV, non-invasive ventilation; PaCO2, arterial partial pressure of carbon dioxide; PaO2, arterial partial pressure of oxygen.

Table 3. Independent predictors of noninvasive ventilation failure.

Variables	Univariable Regression			Multivariable Regression		
	HR	95% CI	p-value	HR	95% CI	p-value
SOFA score	1.53	1.24 – 1.88	0.001*	1.51	1.11 – 2.06	0.009*
Procalcitonin	1.35	1.05 – 2.00	0.048*	-	-	-
CRP	1.03	1.01 – 1.05	0.004*	1.03	1.01 – 1.05	0.003*
Systolic BP	0.96	0.94 – 0.98	<0.001*	-	-	-
Heart rate	1.03	1.01 – 1.06	0.027*	-	-	-
Respiratory rate	1.30	1.15 – 1.48	<0.001*	1.18	1.01 – 1.38	0.039*
EPAP	2.37	1.31 – 4.27	0.004*	-	-	-
				-2Log Likelihood = 122.7, p < 0.001		

The effects of confounder factors such as gender, and comorbidities were adjusted in the multivariable regression analysis. Abbreviations: BP, blood pressure; CI, confidence interval; CRP, C-reactive protein; EPAP, expiratory positive airway pressure; HR, hazard ratio; SOFA, sequential organ failure assessment.

Discussion

This study is among the limited studies assessing factors associated to NIV failure in advanced-age patients hospitalized in the intensive care unit for pneumonia-associated AHRF. Associations were found between NIV failure and several clinical indicators, including elevated SOFA scores, heightened inflammation markers, increased respiratory rates, and higher EPAP settings. Among these potential factors, the SOFA score, CRP levels, and respiratory rate were identified as independent predictors of NIV failure.

Elderly patients are particularly prone to pneumonia, a major cause of respiratory failure that requires admission to ICUs [15, 16]. Additionally, advanced age correlates with less favorable outcomes patients experiencing acute respiratory failure [17-19]. However, there are concerns that NIV failure may be more common in this cohort, which increases hesitations about using NIV in elderly patients affected by pneumonia [20-22]. Despite these challenges, evidence from a randomized controlled trial suggests that NIV can effectively reduce the rates of intubation and mortality compared to high-concentration oxygen therapy in severe pneumonia-induced hypoxemia [23]. Previous studies on AHRF have shown that NIV improves gas exchange, reduces ventilator-associated pneumonia, and is associated with lower complication and mortality rates, as well as shorter durations of IMV and ICU stays. However, endotracheal intubation was reported to be necessary in 31-54% of cases [24, 25]. Therefore, it is recommended to exercise caution when using NIV in AHRF patients at high risk of failure.

In fact, in patients with AHRF, NIV aims to lessen respiratory effort, correct rapid and shallow breathing, and avert respiratory muscle exhaustion and the need for endotracheal intubation [1]. However, studies involving these patients have reported conflicting results. It has also been reported that ICU mortality rates in elderly patients do not differ between NIV and IMV [26, 27]. A previous study included 369 very elderly patients who were hospitalized for community-acquired pneumonia with respiratory failure. Among these patients, 232 (63%) were treated with NIV, while 137 (37%) were treated with invasive mechanical ventilation (IMV) as their initial ventilation strategy. In the mentioned study, hospital mortality was reported as 49% for NIV and 66% for IMV [28]. The heterogeneity of patients included in these studies may lead to varying outcomes for NIV in AHRF. Our study found a mortality rate of 48% among very elderly patients hospitalized for pneumonia with AHRF.

In the present study, NIV failure was observed in all patients who died. The clinical trial results demonstrated that NIV failure was independently linked to poor clinical outcomes, including increased morbidity and mortality [29-33]. In fact, elderly patients are more prone to severe physiological abnormalities and have a higher risk of NIV failure [34]. The success rate of NIV in treating acute respiratory failure associated with pneumonia varies between 20% and 76%, making it challenging to identify which patients will respond well to the treatment [35]. Therefore, recognizing the risk factors for NIV failure is crucial for improving patient outcomes. Moreover, early recognition of these risk factors allows for the optimization of resource allocation within ICUs, ensuring that interventions are both timely and appropriate.

Patients with AHRF, physiological derangement, severe pneumonia, severe hypoxemia, and those over the age of 40 constitute risk factors for NIV failure [24, 36]. Several studies have

suggested that higher SOFA scores, increased expiratory tidal volume, lower pH, elevated heart rate, increased respiratory rate, and lower PaO2/FiO2 are significant predictors of NIV failure [37-41]. In a study conducted on pneumonia patients over 65 years old, it was reported that elevated heart rate, increased PaCO2 and lower PaO2/FiO2 levels after one hour of NIV were independent predictors of NIV failure [41]. In another study involving a similar age group, the independent predictors of NIV failure were identified as the presence of pneumonia, elevated heart rate, and increased PaCO2 levels after one hour of NIV [12]. Supporting these findings on the utility of NIV, a meta-analysis involving patients with AHRF demonstrated that NIV significantly reduces the risk of intubation in patient groups with PaO2/FiO2 ratios between 100 mm Hg and 200 mmHg, as well as in those with ratios between 200 mm Hg and 300 mmHg [7]. This evidence suggests that NIV can be an effective intervention across a broader spectrum of hypoxemia severity than previously recognized, extending its potential applicability in clinical practice.

The specific risk factors for NIV failure in very elderly patients hospitalized for pneumonia with AHRF remain unclear. In the present study, the PaO2/FiO2 ratio was not associated with NIV failure. This may be related to the inclusion of only very elderly AHRF patients, which differs from other studies. Therefore, the PaO2/FiO2 ratio may not provide predictive value in a very elderly AHRF cohort. However, consistent with the aforementioned studies, an increased respiratory rate was a significant predictor of NIV failure. An elevated respiratory rate may indicate increased breathing effort and significant fatigue in the respiratory muscles, making patients more susceptible to NIV failure [22, 42]. It has been demonstrated in numerous studies that patients with higher SOFA scores have a greater likelihood of experiencing NIV failure [38, 39, 43-45]. Our study also supports these findings. In patients with AHRF, the respiratory component of the SOFA score, typically measured by oxygenation indices like the PaO2/FiO2 ratio, is particularly critical. Patients with NIV failure tended to have a decrease in PaO2/FiO2. However, PaO2/FiO2 alone was not found to be a significant parameter. Scoring systems that incorporate combined parameters may serve as better prognostic indicators for very elderly patients with AHRF. Clinical signs and biochemical parameters can serve as early predictors of adverse outcomes in patients with pneumonia. Another predictor of NIV failure was increased CRP levels. In patients with mild to moderate acute respiratory distress syndrome due to pneumonia, those who failed non-invasive ventilation were reported to have higher CRP levels and lower albumin levels [46]. Although there is an increase in the inflammatory response due to infection, an excessive inflammatory response can lead to increased alveolar-capillary barrier permeability, lung edema, and organ damage [47]. This is consistent with higher SOFA scores.

The current study had several significant limitations. It was primarily a single-center, retrospective study and involved a relatively small cohort of subjects. Secondly, the study included only patients over the age of 85. Including patients between the ages of 65 and 85 could have provided better insights into distinguishing factors that potentially affect NIV failure in both elderly cohorts. Thirdly, all patients received oronasal NIV, and different interface types could potentially impact NIV failure rates. Lastly, the study did not include patients with hypercapnic respiratory failure. The inclusion of such patients could have provided a more thorough evaluation of factors influencing NIV failure across different types of respiratory failure.

Conclusion

In very elderly patients with AHRF due to pneumonia, the use of NIV may offer a significant survival benefit if patients are closely monitored and potential risk factors are considered. For predicting NIV failure in this cohort, systemic inflammation parameters, SOFA score, and respiratory rate can be utilized.

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Conflicts of Interest: The authors declare they have no conflicts of interest.

Ethics Approval: The study was performed in accordance with the Declaration of Helsinki, and was approved by the Ethics Committee of the Medical Faculty of the KTO Karatay University (Date: 21.09.2022, Decision No: 2022/042).

Informed Consent: The need for informed consent was waived under the approval of the Local Ethics Committee due to the retrospective design.

Availability of Data and Material: The data that support the findings of this study are available on request from the corresponding author.

Authors' contribution: Concept – K.K., Design- K.K., Data collection and/or processing – K.K., M.S.I., and D.E., Analysis and/or interpretation - K.K., M.S.I., and D.E., Writing – K.K., Critical review- M.S.I., and D.E. All authors read and approved the final version of the manuscript.

References

1. Bello G, De Pascale G, and Antonelli M. Noninvasive Ventilation. Clin Chest Med. 2016;37(4):711-21. DOI: 10.1016/j.ccm.2016.07.011.
2. Popowicz P and Leonard K. Noninvasive Ventilation and Oxygenation Strategies. Surg Clin North Am. 2022;102(1):149-57. DOI: 10.1016/j.suc.2021.09.012.
3. Mas A and Masip J. Noninvasive ventilation in acute respiratory failure. Int J Chron Obstruct Pulmon Dis. 2014;9:837-52. DOI: 10.2147/COPD.S42664.
4. Aswanetmanee P, Limsuwat C, Maneechotesuwan K, and Wongsurakiat P. Noninvasive ventilation in patients with acute hypoxemic respiratory failure: a systematic review and meta-analysis of randomized controlled trials. Sci Rep. 2023;13(1):8283. DOI: 10.1038/s41598-023-35323-0.
5. Group ST. Hypoxemia in the ICU: prevalence, treatment, and outcome. Ann Intensive Care. 2018;8(1):82. DOI: 10.1186/s13613-018-0424-4.
6. Rochwerg B, Brochard L, Elliott MW, et al. Official ERS/ATS clinical practice guidelines: noninvasive ventilation for acute respiratory failure. Eur Respir J. 2017;50(2) DOI: 10.1183/13993003.02426-2016.
7. Xu XP, Zhang XC, Hu SL, et al. Noninvasive Ventilation in Acute Hypoxemic Nonhypercapnic Respiratory Failure: A Systematic Review and Meta-Analysis. Crit Care Med. 2017;45(7):e727-e33. DOI: 10.1097/CCM.0000000000002361.
8. Piroddi IMG, Barlascini C, Esquinas A, Braido F, Banfi P, and Nicolini A. Non-invasive mechanical ventilation in elderly patients: A narrative review. Geriatr Gerontol Int. 2017;17(5):689-96. DOI: 10.1111/ggi.12810.
9. Brochard L, Lefebvre JC, Cordioli RL, Akoumianaki E, and Richard JC. Noninvasive ventilation for patients with hypoxemic acute respiratory failure. Semin Respir Crit Care Med. 2014;35(4):492-500. DOI: 10.1055/s-0034-1383863.
10. Levy M, Tanios MA, Nelson D, et al. Outcomes of patients with do-not-intubate orders treated with noninvasive ventilation. Crit Care Med. 2004;32(10):2002-7. DOI: 10.1097/01.ccm.0000142729.07050.c9.
11. Schettino G, Altobelli N, and Kacmarek RM. Noninvasive positive pressure ventilation reverses acute respiratory failure in select "do-not-intubate" patients. Crit Care Med. 2005;33(9):1976-82. DOI: 10.1097/01.ccm.0000178176.51024.82.
12. Park MJ, Cho JH, Chang Y, et al. Factors for Predicting Noninvasive Ventilation Failure in Elderly Patients with Respiratory Failure. J Clin Med. 2020;9(7) DOI: 10.3390/jcm9072116.
13. Schortgen F, Follin A, Piccari L, et al. Results of noninvasive ventilation in very old patients. Ann Intensive Care. 2012;2(1):5. DOI: 10.1186/2110-5820-2-5.
14. Force ADT, Ranieri VM, Rubenfeld GD, et al. Acute respiratory distress syndrome: the Berlin Definition. JAMA. 2012;307(23):2526-33. DOI: 10.1001/jama.2012.5669.
15. Muir JF, Lamia B, Molano C, and Cuvelier A. Respiratory failure in the elderly patient. Semin Respir Crit Care Med. 2010;31(5):634-46. DOI: 10.1055/s-0030-1265903.
16. Valley TS, Sjoding MW, Ryan AM, Iwashyna TJ, and Cooke CR. Association of Intensive Care Unit Admission With Mortality Among Older Patients With Pneumonia. JAMA. 2015;314(12):1272-9. DOI: 10.1001/jama.2015.11068.
17. Farfel JM, Franca SA, Sitta Mdo C, Filho WJ, and Carvalho CR. Age, invasive ventilatory support and outcomes in elderly patients admitted to intensive care units. Age Ageing. 2009;38(5):515-20. DOI: 10.1093/ageing/afp119.
18. Ma JG, Zhu B, Jiang L, Jiang Q, and Xi XM. Gender- and age-based differences in outcomes of mechanically ventilated ICU patients: a Chinese multicentre retrospective study. BMC Anesthesiol. 2022;22(1):18. DOI: 10.1186/s12871-021-01555-8.
19. Esteban A, Anzueto A, Frutos-Vivar F, et al. Outcome of older patients receiving mechanical ventilation. Intensive Care Med. 2004;30(4):639-46. DOI: 10.1007/s00134-004-2160-5.
20. Scala R. Challenges on non-invasive ventilation to treat acute respiratory failure in the elderly. BMC Pulm Med. 2016;16(1):150. DOI: 10.1186/s12890-016-0310-5.
21. Ferrer M, Cosentini R, and Nava S. The use of non-invasive ventilation during acute respiratory failure due to pneumonia. Eur J Intern Med. 2012;23(5):420-8. DOI: 10.1016/j.ejim.2012.02.011.
22. Ozyilmaz E, Ugurlu A O, and Nava S. Timing of noninvasive ventilation failure: causes, risk factors, and potential remedies. BMC Pulm Med. 2014;14:19. DOI: 10.1186/1471-2466-14-19.
23. Ferrer M, Esquinas A, Leon M, Gonzalez G, Alarcon A, and Torres A. Noninvasive ventilation in severe hypoxemic respiratory failure: a randomized clinical trial. Am J Respir Crit Care Med. 2003;168(12):1438-44. DOI: 10.1164/rccm.200301-072OC.
24. Antonelli M, Conti G, Esquinas A, et al. A multiple-center survey on the use in clinical practice of noninvasive ventilation as a first-line intervention for acute respiratory distress syndrome. Crit Care Med. 2007;35(1):18-25. DOI: 10.1097/01.CCM.0000251821.44259.F3.
25. Antonelli M, Conti G, Rocco M, et al. A comparison of noninvasive positive-pressure ventilation and conventional mechanical ventilation in patients with acute respiratory failure. N Engl J Med. 1998;339(7):429-35. DOI: 10.1056/NEJM199808133390703.

26. Valley TS, Walkey AJ, Lindenauer PK, Wiener R S, and Cooke CR. Association Between Noninvasive Ventilation and Mortality Among Older Patients With Pneumonia. Crit Care Med. 2017;45(3):e246-e54. DOI: 10.1097/CCM.0000000000002076.
27. Carron M, Freo U, BaHammam AS, et al. Complications of non-invasive ventilation techniques: a comprehensive qualitative review of randomized trials. Br J Anaesth. 2013;110(6):896-914. DOI: 10.1093/bja/aet070.
28. Besen B, Park M, and Ranzani OT. Noninvasive ventilation in critically ill very old patients with pneumonia: A multicenter retrospective cohort study. PLoS One. 2021;16(1):e0246072. DOI: 10.1371/journal.pone.0246072.
29. Antonelli M, Conti G, Moro ML, et al. Predictors of failure of noninvasive positive pressure ventilation in patients with acute hypoxemic respiratory failure: a multi-center study. Intensive Care Med. 2001;27(11):1718-28. DOI: 10.1007/s00134-001-1114-4.
30. Nava S and Ceriana P. Causes of failure of noninvasive mechanical ventilation. Respir Care. 2004;49(3):295-303.
31. Nava S and Hill N. Non-invasive ventilation in acute respiratory failure. Lancet. 2009;374(9685):250-9. DOI: 10.1016/S0140-6736(09)60496-7.
32. Confalonieri M, Garuti G, Cattaruzza MS, et al. A chart of failure risk for noninvasive ventilation in patients with COPD exacerbation. Eur Respir J. 2005;25(2):348-55. DOI: 10.1183/09031936.05.00085304.
33. Demoule A, Girou E, Richard JC, Taille S, and Brochard L. Benefits and risks of success or failure of noninvasive ventilation. Intensive Care Med. 2006;32(11):1756-65. DOI: 10.1007/s00134-006-0324-1.
34. Sevransky JE and Haponik EF. Respiratory failure in elderly patients. Clin Geriatr Med. 2003;19(1):205-24. DOI: 10.1016/s0749-0690(02)00065-4.
35. Vanoni NM, Carugati M, Borsa N, et al. Management of Acute Respiratory Failure Due to Community-Acquired Pneumonia: A Systematic Review. Med Sci (Basel). 2019;7(1) DOI: 10.3390/medsci7010010.
36. Watson A, Yadollahi S, Fahmy A, et al. Non-Invasive Ventilation for Community-Acquired Pneumonia: Outcomes and Predictors of Failure from an ICU Cohort. Medicina (Kaunas). 2023;60(1) DOI: 10.3390/medicina60010081.
37. Chen Q, Liu M, Liu B, et al. Predictive Factors for Failure of Noninvasive Ventilation in Adult Intensive Care Unit: A Retrospective Clinical Study. Can Respir J. 2020;2020:1324348. DOI: 10.1155/2020/1324348.
38. Carteaux G, Millan-Guilarte T, De Prost N, et al. Failure of Noninvasive Ventilation for De Novo Acute Hypoxemic Respiratory Failure: Role of Tidal Volume. Crit Care Med. 2016;44(2):282-90. DOI: 10.1097/CCM.0000000000001379.
39. Duan J, Chen L, Liu X, et al. An updated HACOR score for predicting the failure of noninvasive ventilation: a multicenter prospective observational study. Crit Care. 2022;26(1):196. DOI: 10.1186/s13054-022-04060-7.
40. Al-Rajhi A, Murad A, Li PZ, and Shahin J. Outcomes and predictors of failure of non-invasive ventilation in patients with community acquired pneumonia in the ED. Am J Emerg Med. 2018;36(3):347-51. DOI: 10.1016/j.ajem.2017.08.016.
41. Hong Y, Duan J, Bai L, Han X, Huang S, and Guo S. Noninvasive ventilation failure in pneumonia patients >/=65years old: The role of cough strength. J Crit Care. 2018;44:149-53. DOI: 10.1016/j.jcrc.2017.11.008.
42. Scala R and Pisani L. Noninvasive ventilation in acute respiratory failure: which recipe for success? Eur Respir Rev. 2018;27(149) DOI: 10.1183/16000617.0029-2018.
43. Duan J, Chen L, Liang G, et al. Noninvasive ventilation failure in patients with hypoxemic respiratory failure: the role of sepsis and septic shock. Ther Adv Respir Dis. 2019;13:1753466619888124. DOI: 10.1177/1753466619888124.
44. Nicolini A, Piroddi IM, Barlascini C, and Senarega R. Predictors of non-invasive ventilation failure in severe respiratory failure due to community acquired pneumonia. Tanaffos. 2014;13(4):20-8.
45. Rittayamai N, Pravarnpat C, Srilam W, Bunyarid S, and Chierakul N. Safety and efficacy of noninvasive ventilation for acute respiratory failure in general medical ward: a prospective cohort study. J Thorac Dis. 2023;15(10):5466-74. DOI: 10.21037/jtd-23-732.
46. Sun W, Luo Z, Cao Z, Wang J, Zhang L, and Ma Y. A combination of the APACHE II score, neutrophil/lymphocyte ratio, and expired tidal volume could predict non-invasive ventilation failure in pneumonia-induced mild to moderate acute respiratory distress syndrome patients. Ann Transl Med. 2022;10(7):407. DOI: 10.21037/atm-22-536.
47. Abraham E, Carmody A, Shenkar R, and Arcaroli J. Neutrophils as early immunologic effectors in hemorrhage- or endotoxemia-induced acute lung injury. Am J Physiol Lung Cell Mol Physiol. 2000;279(6):L1137-45. DOI: 10.1152/ajplung.2000.279.6.L1137.