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# General ward and pneumonia size as predictors of noninvasive ventilation failure

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**SUMMARY**

**Introduction** Shortage of intensive care beds has led to more frequent use of noninvasive ventilation (NIV) outside respiratory units, and data on NIV efficacy and safety on general wards is lacking.

**Objective** The aim was to identify potential predictors for NIV failure.

**Methods** This was a retrospective analysis of patients treated with NIV at the Institute for Pulmonary Diseases of Vojvodina from 2009 to 2013. Demographics, blood gases, chest radiographs, setting, and outcomes were analyzed to identify predictors of NIV failure.

**Results** A total of 138 patients (65% men, mean age 66 ± 11 years) were treated with NIV. Indications for NIV were acute exacerbation of chronic obstructive pulmonary disease (85%) and cardiogenic pulmonary edema (7%), as well as respiratory insufficiency related to obesity and central hypoventilation (5%) and neuromuscular disease (3%). Rate of NIV failure was 34.8%. In 86 patients NIV was applied in the High Dependency Unit (HDU), while 52 received NIV on the general ward. Baseline characteristics in terms of gender, arterial blood gases, and the extent of consolidation on chest radiographs were similar. Patients treated in HDU were younger (64.4 ± 1.2 vs. 69.4 ± 1.5 years, $p < 0.001$). NIV on the general ward compared to HDU had higher rates of NIV failure (28/52 vs. 20/86, $p < 0.001$). Presence of consolidation involving two or more quadrants on chest radiograph (55% vs. 29%, $p < 0.001$) was associated with NIV failure. When adjusted for age and the extent of consolidation on chest radiograph, NIV failure was still less likely in patients treated in HDU (OR 0.23, 95% CI 0.10–0.50).

**Conclusion** Patients with consolidation on chest X-ray and patients treated with NIV outside of dedicated respiratory units are at a higher risk for NIV failure.

**Keywords**: mechanical ventilation; respiratory care units; noninvasive ventilation; respiratory insufficiency

## INTRODUCTION

Introduction of noninvasive ventilation (NIV) into clinical practice has led to significant reduction in intubation rates and mortality by minimizing the complications related to invasive mechanical ventilation [1–4]. The two leading indications for NIV in daily clinical practice are severe exacerbation of chronic obstructive pulmonary disease (COPD) and acute cardiogenic edema [5, 6]. Immunocompromised patients with acute respiratory failure are also recognized as a group of patients in which NIV is favored over invasive ventilation [2–6].

While previously all patients requiring ventilatory support had to be placed in an intensive care environment, introduction of NIV and a supposed straightforward application of the technique has led to its more frequent use outside of the dedicated respiratory units. Shortage of beds in intensive care units (ICU) and high dependency units (HDU) and the growing need for ventilatory support justify this approach. Also, early use of NIV, which translates into the initiation of NIV in an emergency department, has been proposed to improve final outcome [7].

Many studies attempted to identify potential predictors of NIV success [8–13], but only a few actually compared the outcome with regard to the setting in which NIV was applied [14, 15, 16]. The data on NIV efficacy and safety outside respiratory units is lacking, and our study is aimed to evaluate the use of NIV on general ward compared to HDU and help define potential early predictors on NIV failure.

## OBJECTIVE

The aim of this study was to identify potential predictors for NIV failure.

## METHODS

This was a retrospective observational study which included patients treated with NIV at the Institute for Pulmonary Diseases of Vojvodina, Sremska Kamenica, Serbia, between June 2009 and February 2013. NIV was used sporadically in our five-bed ICU opened in 2003, and then routinely since the opening of a six-bed HDU in 2009. Local protocol was developed, and NIV was initiated in patients requiring ventilatory support, without predefined contraindications for NIV [4, 5 ,6]. ICU/HDU staff conducted the training of medical staff on general wards with the intention of introducing NIV outside of ICU/HDU in

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instances where there were no available beds in dedicated respiratory units. NIV was initiated by ICU/HDU staff and then followed up by the medical staff on general wards. Continuous pulse oximetry was recommended, and NIV list was attached to patient's chart in order to regularly check for heart rate, respiratory rate, level of consciousness, basic ventilator settings (IPAP/EPAP/FiO2), and change in blood gas values after 30–60 minutes, and then as ordered by the attending physician.

Demographics, blood gas analysis, chest radiographs, indications for NIV, the setting where NIV was applied, and final outcomes were extracted from the medical records and analyzed to identify potential predictors of NIV failure defined as intubation or death. Since this was a retrospective analysis, the patients' informed consent was waived, in accordance with the decision of the Institute Ethics Committee.

Continuous data are presented as means and standard deviation for normally distributed data, and median and interquartile range for non-normally distributed data. Categorical variables are presented as whole numbers and percentages. The comparison of variables was done using Mann–Whitney U-test and Fisher's exact test, as appropriate. Predictors of NIV failure were examined in univariate, followed by multivariate logistic regression model. Only variables that were significant in univariate model were included in the multivariate model. A probability of $p < 0.05$ was considered statistically significant.

## RESULTS

Our study included 138 patients who were treated with NIV, and their mean age was 66 ± 11 years. There were 80 (58%) male patients. Most frequent indications for NIV were severe acute exacerbation of COPD with respiratory acidosis (85%) and cardiogenic pulmonary edema (7%). There were also 5% of patients with obesity and central hypoventilation and 3% with neuromuscular disease.

In 86 patients (62%) NIV was applied in the HDU, while the remaining 52 received NIV on the general ward. The selection was based on availability of HDU beds – if there was no available bed in the dedicated respiratory unit at the time, the patient was ventilated on the general ward.

Baseline characteristics of the two groups of patients in terms of gender, initial arterial blood gas values (pH, $PaCO_2$, $PaO_2$), and the extent of consolidation on chest radiographs were similar. However, patients treated in HDU were younger (64.4 ± 1.18 vs. 69.4 ± 1.51, $p < 0.001$). (Table 1)

Overall rate of NIV failure was 34.8%. NIV on general ward compared to NIV in HDU had higher rates of failure (20/86 vs. 28/52, $p < 0.001$).

Presence of consolidation involving two or more quadrants on chest radiograph (55% vs. 29%, $p < 0.001$) was also associated with NIV failure.

Multivariate analysis results showed that, when adjusted for age and the extent of consolidation on chest radiographs, NIV failure was still less likely in patients treated in HDU (OR 0.23, 95% CI 0.10–0.50). **(Table 2)**

**Table 1.** Patients' baseline characteristics and outcome – HDU vs. general ward

| | HDU n = 86 | General ward n = 52 | p |
|---|---|---|---|
| Age (mean ± SD) | 64.37 ± 11.63 | 69.38 ± 9.56 | 0.01 |
| Male n (%) | 57 | 60 | 0.86 |
| pH (mean ± SD) | 7.26 ± 0.08 | 7.27 ± 0.01 | 0.37 |
| $PCO_2$ (mean ± SD) | 9.50 ± 2.31 | 9.86 ± 1.91 | 0.34 |
| $PO_2$ (mean ± SD) | 6.76 ± 2.21 | 6.07 ± 2.24 | 0.08 |
| Consolidation on ≥ 2 quadrants n (%) | 23 | 17 | 0.52 |
| NIV failure n (%) | 23 | 54 | < 001 |

HDU – high dependency unit;
$PCO_2$ – partial pressure of carbon dioxide;
$PCO_2$ – partial pressure of oxigen

**Table 2.** Multivariate analysis of potential predictors of NIV failure

| | Odds ratio | 95% confidence interval |
|---|---|---|
| Age | 1.03 | 0.09–11.45 |
| Consolidation on ≥2 quadrants | 3.97 | 1.60–10.33 |
| HDU | 0.23 | 0.10–0.50 |

NIV – noninvasive ventilation

## DISCUSSION

NIV is a well established treatment modality for severe exacerbation of COPD [1–6]. According to the Cochrane review with fourteen randomized controlled trials, introduction of NIV significantly reduced intubation rates and mortality [17]. Similarly, the Cochrane review on the use of NIV for acute cardiogenic pulmonary edema covered as many as 21 studies, and the conclusion was that the addition of NIV brings about significant decline in intubation rates and hospital mortality [18].

While there is no question that NIV should be used for appropriate indications, there are many questions as to where it can be safely used, what the basic pre-requirements for such setting are, and how to timely recognize NIV failure. British Thoracic Society guidelines on the use of NIV in acute COPD exacerbations concisely state that "NIV should be delivered in a dedicated setting that could include an acute medical ward, accident and emergency, high dependency unit or a critical care area" [19]. That largely depends on internal organization of a hospital and what they established as a "dedicated setting." More importantly, it is said that "acute NIV should only take place in a setting where escalation to intubation and (invasive) ventilation is available" [19]. This provision clearly limits a potential setting where NIV could be performed to an area in close proximity to ICU. In our hospital, six-bed High Dependency Unit was opened in 2009 next to the ICU. Initially, all patients requiring NIV were ventilated either in ICU or HDU. However, with increasing demand for ventilatory support, on many occasions patients had to be ventilated on general wards. We developed a local protocol for NIV, according to which NIV was initiated in all patients requiring ventilatory support, without predefined contraindications. ICU/HDU staff conducted the training of medical staff on general respiratory wards. NIV was as

a rule initiated by ICU/HDU staff and then followed up by the medical staff on general wards. Results of our study showed that NIV failure rate on general wards was significantly higher than in HDU. This differs from the results of a multicenter controlled trial by Plant et al. [14], where the authors concluded that NIV can be safely used on a general ward with a satisfactory outcome. There was also an interesting pilot study by Cabrini et al. [15], who advocated that NIV outside dedicated respiratory units should be managed exclusively by medical emergency teams – in this study 77% of patients avoided intubation. Conflicting results of these two studies may implicate that the proposed policies for the use of NIV outside the dedicated respiratory units largely depend on internal resources and organization of any given institution. Another observational study by Farha et al. [16] showed similar success rates for NIV on a regular ward and in the ICU. Still, all listed authors urge caution and careful patient selection, and list many necessary pre-requirements for the application of NIV outside ICU. That is why at the Massachusetts General Hospital there is an extensive NIV checklist to help select patients who need to be transferred to the ICU as soon as possible [20].

It is difficult to predict which patients will do well on NIV, but Confalonieri et al. [8] found that NIV failure was more likely in patients with more severe respiratory acidosis, higher age, lower level of consciousness, and higher respiratory rate. In our study degree of respiratory acidosis and age did not predict outcome, but the presence of consolidation on chest radiograph did. These results are similar to the results of Antonelli et al. [9], who found that presence of pneumonia was a negative prognostic factor for patients on NIV.

Another concern is that the patients who require invasive ventilation after NIV failure have higher hospital mortality [21]. It is, therefore, crucial to timely recognize NIV failure. In attempt to conclude why our patients on general wards had poorer outcome, we propose two possible explanations. The first is that the level of monitoring that the patients on NIV require cannot be satisfactorily delivered on our general wards. Even though we made a checklist of the necessary parameters, monitoring was not continuous, in contrast to HDU, and often the first signs of failure or the need to readjust parameters were not timely recognized.

The second potential explanation for our results is the assumption that greater clinical NIV expertise allows better titration of NIV parameters and provision of more adequate ventilatory support. Even if NIV was initiated by ICU/HDU staff, subsequent titration and readjustments may not have been done in a timely manner and by experienced staff.

Main limitation of our study is that it was a retrospective analysis, which did not allow precise insight into all the parameters possibly related to the causes of NIV failure.

## CONCLUSION

Patients treated with NIV on general wards are at a higher risk for ventilation failure than patients treated in HDU. Presence of consolidation involving two or more quadrants on a chest radiograph in our study was also associated with NIV failure. Medical staff inexperience and the lack of resources for adequate level of monitoring may preclude successful NIV application on a general ward even in a tertiary care center. Developing internal NIV protocols suited to the resources of each individual hospital may be a temporary solution until there are enough studies to adopt evidence-based guidelines for the adequate use of NIV on general wards.

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# Опште одељење и величина пнеумоније као предиктори неуспеха неинвазивне вентилације

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**КРАТАК САДРЖАЈ**

**Увод** Недостатак места у јединицама интензивне неге резултирао је учесталом применом неинвазивне вентилације (НИВ) ван респираторних јединица, а подаци о безбедној употреби НИВ-а на општим одељењима су оскудни.

**Циљ** Циљ овог рада био је идентификација потенцијалних предиктора за неповољан исход НИВ-а.

**Методе** Ради се о ретроспективној анализи пацијената лечених у Институту за плућне болести Војводине 2009–2013. године. Анализирани су: демографски подаци, параметри гасних анализа артеријске крви, радиограми грудног коша и болничко одељење на ком је НИВ примењиван, како би се одредили потенцијални предиктори у односу на коначни исход.

**Резултати** Укупно је укључено 138 болесника (65% мушкараца, просечна старост 66 ± 11 година). Индикације за НИВ биле су акутне егзарцебације ХОБП-а (85%), кардиогени плућни едем (7%), као и респираторна инсуфицијенција у склопу гојазности и централне хиповентилације (5%), те неуромускуларних болести (3%). НИВ је био неуспешан код 34,8% болесника. Код 86 болесника НИВ је примењен на полуинтензивној нези (ПИН), док су 52 болесника вентилирана на општем одељењу. Полазне карактеристике биле су сличне – није било статистички значајних разлика у параметрима гасне размене, полу, као ни присуству консолидација на радиограму грудног коша. Болесници третирани на ПИН били су млађи (64,4 ± 1,2 наспрам 69,4 ± 1,5 година, $n < 0,001$). НИВ је био неуспешнији код болесника на општем одељењу (28/52 наспрам 20/86, $n < 0,001$). Присуство консолидације на два или више квадраната на радиограму грудног коша је корелирало са неуспехом НИВ-а (55% наспрам 29%, $n < 0,001$). И након корекције у односу на старост и консолидације, примена НИВ-а на општем одељењу носи статистички значајно повишен ризик за неуспешан исход. (*OR* 0,23, 95% *CI* 0,10–0,50).

**Закључци** Присуство консолидација на радиограму грудног коша и примена неинвазивне вентилације ван респираторних јединица повећавају ризик од неуспешне примене НИВ-а.

**Кључне речи**: механичка вентилација; јединице за респираторну негу; неинвазивна вентилација; респираторна инсуфицијенција

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