Original Article

ISSN: 1735-0344 *Tanaffos 2014; 13(4): 20-28*

TANAFFOS

Predictors of Non-Invasive Ventilation Failure in Severe Respiratory Failure Due to Community Acquired Pneumonia

Antonello Nicolini [1], Ines Maria Grazia Piroddi [1], Cornelius Barlascini [2], Renata Senarega [3]

[1] Respiratory and Internal Medicine Department ASL4 Chiavarese, Italy, [2] Public Health Department ASL4 Chiavarese, Italy, [3] Department of Radiology ASL 4 Chiavarese, Italy.

Received: 9 October 2014
Accepted: 5 November 2014

Correspondence to: Nicolini A
Address: Respiratory and Internal Medicine Department, ASL4 Chiavarese
Via Terzi 43, 16049 Sestri Levante, Italy.
Email address: chiccanene@libero.it

Background: Non-invasive ventilation (NIV) has been used for acute respiratory failure to avoid endotracheal intubation and intensive care admission. Few studies have assessed the usefulness of NIV in patients with severe community acquired pneumonia (CAP). The use of NIV in severe CAP is controversial because there is a greater variability in success compared to other pulmonary conditions.

Materials and Methods: We retrospectively followed 130 patients with CAP and severe acute respiratory failure (PaO2/FiO2 < 250) admitted to a Respiratory Monitoring Unit (RMU) and underwent NIV. We assessed predictors of NIV failure and hospital mortality using univariate and multivariate analyses.

Results: NIV failed in 26 patients (20.0%). Higher chest X-ray score at admission, higher heart rate after 1 hour of NIV, and a higher alveolar-arteriolar gradient (A-aDO2) after 24 hours of NIV each independently predicted NIV failure.

Higher chest X ray score, higher LDH at admission, higher heart rate after 24 hours of NIV and higher A-aDO2 after 24 hours of NIV were directly related to hospital mortality.

Conclusion: NIV treatment had high rate of success. Successful treatment is related to less lung involvement and to early good response to NIV and continuous improvement in clinical response.

Key words: Community-acquired pneumonia, Severe respiratory failure, Non-invasive ventilation, Hospital mortality

INTRODUCTION

Few studies have assessed the usefulness of NIV in patients with severe CAP. Nevertheless, predictors of NIV failure have been reported in different studies (1-5). Recently, Carrillo et al. noted these risk factors for NIV failure: radiographic worsening infiltration 24 hours after admission, maximum sepsis-related organ failure assessment (SOFA) score at admission and after 1 hour of NIV, higher heart rate, lower PaO_2/FIO_2 and bicarbonate (2).

The debate concerning the use of NIV for treatment of severe CAP increased during H1N1 pandemic. Initially, NIV was felt to be contraindicated because of a hypothetical risk of spreading the infection. This hypothesis was refuted by Simmonds et.al. who found that

the droplets generated during NIV are > 10 μm; these are unlikely to be airborne (6).

Over time, NIV success increased (7,8). The success rate was as high as 76% with avoidance of intubation and fewer associated infection complications (e.g., sepsis, septic shock and/or catheter-related infections (6). However, despite good outcomes in H1N1 patients and more recent randomized studies on the use of helmet continuous positive airway pressure (CPAP) versus oxygen therapy in severe hypoxemic respiratory failure due to pneumonia, in which the technique reduced the intubation rate (9,10), the efficacy of NIV in pneumonia has not been definitively established (11). Predictors of NIV failure have not been well defined (12). From our long experience with NIV, we learned that appropriate patient selection is the key to success (13).

The aim of this study was to evaluate the efficacy of NIV and factors related to its failure and mortality in patients with CAP and severe acute respiratory failure (ARF).

MATERIALS AND METHODS

We retrospectively followed 130 consecutive patients with severe ARF due to CAP defined as the ratio of arterial oxygen tension to inspired oxygen fraction (PaO_2/FIO_2) <250 receiving NIV treatment in the RMU of Sestri Levante Hospital, from June 2005 to July 2014. The RMU has four non-invasive monitored beds and admits patients with severe respiratory failure who need non-invasive ventilation. The RMU has both ventilators specifically designed for NIV and invasive ventilation (IMV). Our units can switch to invasive measures e.g., intubation and intensive care unit (ICU) admission quickly.

This study received the approval of Ethics Committee of ASL4 Chiavarese, Italy (n°302) and was carried out in accordance with the Helsinki Declaration. All the patients gave informed consent for NIV treatment and for the study.

Pneumonia was defined as a new pulmonary infiltrate on the admission chest radiograph with symptoms and signs of lower respiratory tract infection according to the American Thoracic Society and Infectious Disease Society of America (IDSA/ATS) guidelines (2,7).

Patients' degree of disease severity and organ failure were estimated using Simplified Acute Physiology Score (SAPS)-II and Confusion, Elevated Blood Urea Nitrogen, Respiratory Rate and Blood pressure plus Age ≥65 years (CURB65) score (2). The exclusion criteria were any degree of immunosuppression, lack of spontaneous breathing, gasping, anatomical evidence of functional airway obstruction and gastrointestinal bleeding, or ileus, massive agitation, severe hypoxemia or acidosis (pH<7.10) (2,14,15). Upon admission, all patients received empirical antimicrobial therapy according to the IDSA/ATS guidelines (16).

Upon admission, specific urinary tests for Streptococcus pneumonia and Legionella pneumophila as well as blood culture were performed for all patients.

The indication for NIV use followed an established protocol: moderate to severe dyspnea accompanied by respiratory rate ≥ 30 breaths/m, signs of respiratory distress (e.g. use of accessory respiratory muscles), (PaO_2/FiO_2) < 250 (2,13-15).

The inability of patient to adapt himself/herself to the device or unwillingness to undergo NIV was considered a contraindication for NIV.

Patients were ventilated using pressure support ventilation (PSV) or bi-level- ST ventilation (BIPAP).

The following parameters were recorded upon admission: age, sex, co-morbidities, number of lobes involved on chest x-ray or on chest computed tomography (CT), Opravil radiological score (17), PaO2 on room air, PaCO2, pH, PaO2/FIO2 ratio, alveolar-arterial gradient (A-aDO2), Simplified Acute Physiology Score (SAPS) II, Kelly-Matthay scale, ventilation mode, setting of mechanical ventilator and PaO2/FIO2 after 1 hour of non-invasive

ventilation. If a patient who underwent NIV did not experience an improvement of PaO2/FIO2 ratio of more than 175 after 1 hour of continued NIV, and/or if one or more complications occurred (neurological impairment, persistence of dyspnea and tachypnea, hemodynamic instability and intolerance of the interface, the patient was considered to have failed NIV and IMV was initiated. EPAP or PEEP (positive end expiratory pressure) was set initially at 5 cm H2O and the level was raised by 1-2 cm H2O if needed to achieve PaO2 > 60 mmHg or SpO2 of > 90%. Inspiratory pressure ventilation was increased, starting from 10 cmH2O, in increments of 2-3 cmH2O to obtain a tidal volume (VT) of 6-8 ml/Kg and a respiratory rate < 30 breaths/m'. Conversely, NIV was deemed successful when respiratory failure improved and the patient did not feel the need for more than 48 hours of ventilator treatment having a PaO2/FiO2 ratio > 250 with spontaneous breathing (3,13).

Primary outcomes:

NIV failure and hospital mortality were the primary outcomes.

Secondary outcomes:

Changes in arterial blood gases (ABG) analysis at admission and after 1 hour of NIV, NIV duration and the length of hospital stay were the secondary outcomes.

Statistical analysis:

Continuous variables expressed as mean ± standard deviation were compared with the regression analysis corrected for age. Categorical variables expressed as number and percentages were compared using chi-square test. A P-value ≤0.05 was considered significant. The predictors identified as predictors of NIV failure and hospital mortality were analyzed initially with univariate regression analysis and therefore, were also included in a multivariate logistic regression analysis. Adjusted odds ratios (OR) and 95% confidence interval (CI) were computed for variables independently associated with NIV failure or hospital mortality. The predictive capacity for NIV failure or hospital mortality of quantitative variables was assessed with receiver-operating characteristic (ROC) curves; the area under the curve (AUC), optimal cut-off values, sensitivity, specificity and positive and negative predictive values were calculated. Data analysis was made with statistical software R-Project version 2.13.2.

RESULTS

One hundred and thirty patients admitted with CAP received NIV (76 males and 54 females aged 59.74±16.17 years) for 90±96 hours, i.e., 3.7±3.3 days (mean ± SD). During NIV treatment, the pressure support ventilation (PSV) was 11±5 cm H2O and PEEP was 8±4 cmH2O. NIV was successfully used in 104 patients (80.0 %). Twenty-six patients experienced NIV failure; 18 were intubated and admitted to ICU. Eight other patients had previously stated that they did not want to be intubated and died. The main reasons for intubation were worsening of respiratory insufficiency (10 patients), cardio-respiratory arrest (four patients), and multi-organ failure (four patients).

Eight patients who were not intubated died because of multi-organ failure (three patients) and worsening of respiratory failure (five patients).

Acute respiratory failure de novo:

Acute respiratory failure *de novo* was considered as a separate entity (2) in which CAP occurred in patients with no previous cardio-respiratory co-morbidities. Patients in the *de novo* group who failed NIV had more severe scores (CURB 65 and SAPS II), more extensive radiological findings (Opravil score), and more severe respiratory impairment at admission (lower PaO_2/FiO_2 ratio and higher $A\text{-}aDO_2$). They also presented with worse oxygenation and gas exchange, along with a higher respiratory rate after 1 h of NIV and after 24 hours. Moreover, at admission they presented with higher values of LDH and C-reactive protein. Patients who demonstrated NIV success had a SAPS II ≤ 34 and PaO_2/FiO_2 after 1 hour of NIV > 175, previously indicated marker of NIV success (P≤0.001) (4) as well as lower $A\text{-}aDO_2$ after 1 hour of NIV and after 24 hours.

Patients with previous cardiac or respiratory disease were older and had higher $PaCO_2$ and bicarbonate, lower arterial pH and decreased consciousness at admission. But the only significant difference with the *de novo* respiratory failure group was in age (73.±15 versus 47±16 years, P≤0.001) (Table 1).

Table 1. Clinical and ventilatory characteristics of the two groups

	De novo ARF 56 pts		Previous CR ARF 74 pts		P-value
	Mean	Sd.	Mean	Sd.	
age	47	*16*	73	*15*	*<0,001*
Male	38		41		*0.33*
Female	18		33	*15,5*	*0.21*
SAPS II	21	*10*	33	*11*	0.31
Lobes (number)	3	*1*	3	*1*	0.93
Chest X ray score*	8	*3*	8	*3*	0.99
RMU STAY (hours)	162	*119*	116	*136*	0.74
CURB65	1	*1*	2	*1*	0.33
HCO_3	23	*1*	27	*7*	0.33
C-R Prot	22	*9*	22	*9*	0,25
LDH	439	*211*	576	*522*	0.07
Respiratory rate	32	*4*	32	*7*	0.14
Heart rate	103	*11*	105	*14*	0.67
PaO_2	48,50	*12*	55	*15*	0.13
$PaCO_2$	44	*27*	60	*40*	0.47
pH	7,40	*0,10*	7,35	*0,11*	0,27
PaO_2/FiO_2	162	*48*	162	*45*	0.99
A-aDO_2	121	*92*	127	*102*	0.80
KMS	1	*1*	2	*1*	0.12

ARF Acute respiratory failure ; CR cardiac-respiratory disease ; *Opravil chest X-ray score SAPS II = Simplified acute physiology score ; CURB 65 = confusion, elevated blood urea,respiratory rate,blood pressure plus age≥65 years ; A-aDO_2 = Alveolar-arteriolar gradient ; RMU STAY =Length of stay in High-dependency Respiratory Unit; KMS = Kelly-Matthay Scale

Patients in the ARF group did not have significant differences at admission and showed only a drop in respiratory rate and heart rate after 1 hour of NIV in patients with NIV success. In those who failed NIV there was a significant increase of A-aDO_2 after 24 hours in patients (P≤0.02) (Table 2). In multivariate analysis of predictors associated with NIV failure in the two groups, a higher heart rate after 1 hour, a higher A-aDO2 after 24 hours, and a higher X-ray score Opravil score) at admission predicted failure (Table 3).

Survival:

Hospital survivors had less pulmonary involvement as assessed by X ray (Opravil) score, a lower LDH at admission, a greater improvement of respiratory and heart rate after 24 hours of NIV and a better PaO_2/FiO_2 and A-aDO_2 after 24 hours compared with those who died.

In patients with *de novo* ARF survival was also related to A-aDO_2 at admission and after 1 hour of NIV as well as initial C-reactive protein. In patients with previous cardiac and respiratory disease, ARF survival was also associated with a lower severity score at admission (CURB 65 and SAPS II), lower $PaCO_2$ and higher pH after 24 hours of NIV along with a lower respiratory rate after 1 hour of NIV. There was no significant difference between NIV duration or length of stay in the RMU among patients with NIV success or NIV failure (Table 4). In total population, the multivariate analysis identified a higher LDH at admission, a higher X-ray score (Opravil) at admission, higher heart rate after 24 hours and higher A-aDO_2 after 24 hours as independent predictors of hospitality mortality (Table 5). Figure 1 shows the predictors of hospital mortality using ROC curves.

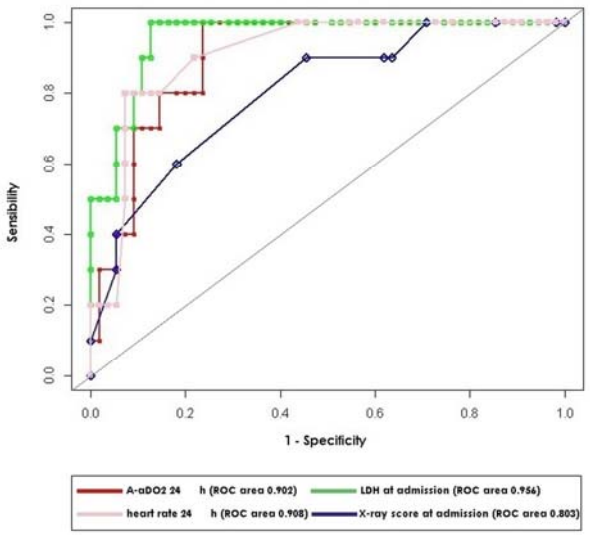

Figure 1. Performance predictive of mortality of the scores evaluated using ROC curves.

Table 2. Variables associated with failure of non-invasive ventilation in the two groups

		« De novo »ARF					Previous cardiac or respiratory ARF					
		NIV success (46)		Failure (10)			NIV success(58)		Failure (16)			
	Time	Mean	Sd	Mean	Sd	P value	Mean	Sd	Mean	Sd	P value	
	0	99,83	78,33	238,2	52,21	<0,001	130,6	114,49	73,25	50,01	0,33	
A-aDO_2	1	162,9	57,38	269,6	199,66	0,03	124,7	96,45	114,5	90,25	0,8	
	2	21,35	23,85	170	90,83	<0,001	70,61	117,9	213,3	68,37	0,02	*
CURB65	0	1,22	0,52	1,8	0,45	0,03	2,21	1,19	2,5	0,58	0,64	
	0	103,1	10,2	108	4	0,3	104,6	13,31	110,8	13,1	0,4	
Heart rate	1	92,48	8,03	111,8	11,23	<0,001	95,82	9,54	109,8	13,33	0,01	*
	2	82,39	8,98	120,8	5,93	<0,001	87,06	13,56	116	19,11	<0,001	*
C-R prot.	0	19,65	8,1	37,8	5,22	<0,001	20,18	8,06	22	6,48	0,67	
LDH	0	343,9	111,86	819,4	149,14	<0,001	518,9	505,17	841,3	295,7	0,22	
	0	182,1	49,38	117,4	14,72	0,008	170	43,25	170,8	43,37	0,9	
PaO_2/FiO_2	1	199,7	43,34	121,4	45,99	0,001	220,9	62,68	217,5	69,23	0,92	
	2	376,9	62,85	176	122,19	<0,001	283,9	80,12	193	145,82	0,06	
	0	43,09	23,59	48,8	18,14	0,6	61,61	45,27	46,75	17,8	0,5	
$PaCO_2$	1	40,0	15,29	40,8	9,52	0,92	51,73	25,95	49	21,32	0,82	
	2	38,83	7,3	45	15,57	0,2	45,91	14,49	60,5	26,56	0,09	
	0	7,4	0,11	7,37	0,08	0,6	7,33	0,17	7,4	0,09	0,5	
pH	1	7,41	0,07	7,42	0,08	0,8	7,35	0,11	7,4	0,11	0,4	
	2	7,4	0,03	7,42	0,1	0,3	7,38	0,08	7,35	0,13	0,6	
	0	31,78	3,29	34	3,74	0,2	32,85	7,14	35,5	5,26	0,5	
Resp. rate	1	25,17	2,66	33,2	3,7	<0,001	27	4,03	34,5	4,12	0,001	*
	2	20,87	4.24	31,4	3,85	<0,001	20,09	2,2	33,7	5,91	<0,001	*
SAPS II	0	19,13	8,68	32	9,38	0,006	34,12	12,07	29,75	14,57	0,5	
Chest X ray score	0	8	2,32	10,6	1,34	0,02	7,24	2,33	10	3,16	0,04	*

0 At admission

1 After 1 hour of NIV

2 After 24 hours of NIV

SAPS II = Simplified acute physiology score

CURB 65 = confusion, elevated blood urea, respiratory rate, blood pressure plus age≥65 years

A-aDO_2 = Alveolar-arteriolar gradient

RMU STAY =Length of stay in Respiratory Monitoring Unit

C-R prot. = C reactive protein

*Variable entered into a multivariate logistic regression analysis

Table 3. Multivariate analysis of variables independently associated with non invasive ventilation failure in the total population

Variables	T	Label	Adj.OR	95% CI		P-value	AUC	Optimal cut-off	Sensitivity (%)	Specificity (%)	Likelihood ratio		Predictive value	
											Positive	Negative	Positive	Negative
A-aDO_2	2	NIV fail	214	19.4	12051	<0.001	0.885	131	88.90	92.90	12.44	0.12	66.7	98.1
heart_rate	1	NIV fail	12.75	2.6	69.4	0.002	0.862	108	55.60	91.11	6.22	0.49	50.0	92.7
X-ray score	0	NIV fail	14.13	2.5	92.1	0.003	0.821	11	44.40	96.40	8.30	0.59	57.1	91.4

NIV fail = Non invasive ventilation failure

A-aDO_2= Alveolar-arteriolar gradient

X-ray score= Chest X ray score (Opravil)

T 0 at admission

T1 after 1hour of NIV

T2 after 24 hours of NIV

Adj OR = Adjusted odds ratio

CI = confidence interval

AUC = area under the curve

Table 4. Variables associated with hospital mortality in the two groups

		« De novo »ARF					Previous cardiac or respiratory ARF					
		Alive (52)		Dead (4)			Alive (58)		Dead (16)			
	time	mean	sd	mean	sd	*p* value	mean	sd	mean	sd	*p* value	
	0	114,4	85,0	256,5	79,9	0.03	106,5	76,1	189,4	182,6	0.06	
A-aDO_2	1	170,7	58,9	327,5	382,5	0.03	122,1	65,2	129,1	170,4	0.9	
	2	37,0	60,2	190,0	48,1	0.002	53,4	69,9	204,1	189,9	0.001	*
CURB65	0	1,3	0,5	2,0	0,0	0.07	2,0	1,1	3,0	0,8	0.03	
	0	104,0	9,9	104,0	0,0	1	103,9	12,4	110,4	15,8	0.2	
Heart rate	1	95,7	11,7	99,5	0,7	0.6	95,2	9,3	105,0	12,7	0.02	
	2	87,2	16,0	116,0	5,7	0.02	84,2	10,8	112,0	16,3	0.001	*
C-R Prot	0	21,8	9,9	37,0	4,2	0.04	20,4	8,1	20,4	7,6	0.9	
LDH	0	389,0	168,7	946,5	62,9	0.001	396,4	177,9	1124,1	810,0	0.001	*
	0	174,5	51,5	120,0	0,0	0.2	170,3	43,4	169,3	42,9	0.9	
PaO_2/FiO_2	1	190,0	49,4	130,0	84,9	0.1	225,9	60,2	201,0	70,4	0.3	
	2	356,1	94,6	145,0	77,8	0.005	300,7	68,3	177,9	102,6	0.001	*
	0	43,2	22,4	55,5	30,4	0.5	57,9	41,5	67,8	51,3	0.6	
PaCO2	1	39,8	14,6	44,5	12,0	0.7	49,7	26,4	57,6	21,0	0.4	
	2	38,8	7,4	54,5	21,9	0.02	43,8	10,8	61,0	25,3	0.006	
	0	7,4	0,1	7,3	0,1	0.4	7,4	0,1	7,3	0,3	0.2	
pH	1	7,41	0,07	7,44	0,1	0.6	7,37	0,1	7,31	0,1	0.1	
	2	7,40	0,04	7,38	0,1	0.4	7,39	0,0	7,30	0,1	0.004	
	0	32,2	3,4	32,0	5,7	0.9	32,0	7,0	37,3	5,0	0.06	
Resp. rate	1	26,3	4,2	30,0	2,8	0.2	26,4	3,7	32,9	4,1	0.001	
	2	22,0	5,2	33,0	1,4	0.006	20,3	3,7	26,1	6,8	0.002	*
SAPS II	0	20,8	9,7	30,0	14,1	0.2	30,8	9,0	44,1	16,9	0.004	
Chest X- ray score	0	8,3	2,3	11,0	1,4	0.1	6,9	2,3	9,9	2,2	0.002	

0 At admission
1 After 1 h NIV
2 After 24 h NIV

SAPS II = Simplified acute physiology score
CURB 65 = confusion, elevated blood urea, respiratory rate, blood pressure plus age≥65 years
A-aDO_2 = Alveolar-arteriolar gradient
RMU STAY =Length of stay in Respiratory Monitoring Unit
C-R prot = C reactive protein

* Variable entered into a multivariate logistic regression analysis

Table 5. Multivariate analysis of variables independently associated with hospital mortality in the total population

Variables	T	Label	Adj OR	95% CI		P value	AUC	Optimal cutoff	Sensitivity (%)	Specificity (%)	Likelihood ratio		Predictive value	
											Positive	Negative	Positive	Negative
A-aDO2	2	H mort	1107.1	7.1	880.0	0.03	0.902	247	30.00	98.20	16.50	0.71	75.0	88.5
Heart rate	2	H mort	6815.2	42.0	770.0	0.03	0.908	108	80.00	92.70	11,00	0.22	66.7	96.2
LDH	0	H mort	31.7	3.1	93.2	0.01	0.956	728	60.00	94.50	13.40	0.42	68.4	92.9
X ray score	0	H mort	12.6	0.9	34.1	0.04	0.803	11	40.00	94.50	7.33	0.63	57.1	90.7

A-aDO_2=Alveolar-arteriolar gradient
T0 at admission
Adj OR = Adjusted odds ratio
AUC = Area under the curve

X-ray score= Chest X-ray (Opravil)
T2 after 24 hours of non-invasive ventilation
CI = Confidence interval

DISCUSSION

Patients with severe respiratory failure due to CAP and previous cardiac or respiratory disease usually have a better response to NIV than patients with *de novo* acute respiratory failure (as demonstrated in previous studies) (2,18,19). Few studies have investigated the benefits of NIV in patients with severe CAP: the oldest showed good results principally in patients with chronic obstructive pulmonary disease (COPD) and hypercapnic respiratory failure (18). Subsequent researches demonstrated that NIV was effective in decreasing the rates of intubation and mortality compared with

high concentration oxygen therapy (9,10,20). Another recent investigation examined patients with ARF *de novo* and ARF due to cardiac or respiratory disease; this study showed that NIV is a safe and effective modality. In patients with ARF *de novo*, NIV failure was associated with a high mortality (2).

Three recent studies (21-23) support the effectiveness of NIV in severe CAP. The first evaluated 151 COPD patients requiring ICU admission, who underwent NIV and reported a failure rate of 31.1%. Nearly 70% of patients has success with NIV. Non-invasive ventilation, hypertension and corticosteroid treatment were associated with decreased mortality; whereas bilateral infiltration, length of ICU stay and duration of IMV were associated with increased mortality (21). The second study included a cohort of 1,946 elderly immunocompromised patients. Unexpectedly, patients who underwent NIV had decreased mortality at 90 days when compared to those treated with invasive mechanical ventilation. The authors concluded that data obtained suggest that physicians should consider the use of NIV for the elderly immunocompromised patients hospitalized with pneumonia. It seemed that patients receiving NIV fared no worse than similar patients receiving IMV (22). The third study reported a similar NIV success rate (75%) related to early use of NIV and to strict patient selection protocol (23).

Only a few studies evaluated the interrelations of radiographic findings and the need for mechanical ventilation in patients admitted with pneumonia (24,25). Erdem et al. demonstrated that patients with bilateral pulmonary involvement most often needed NIV while those with multi-lobar involvement more frequently required IMV (25). A final consideration concerning a high rate of NIV success (80%): the success begins in the emergency department where a strict selection protocol is followed. For example, a patient with PaO_2/FIO_2ratio < 150 was not considered for NIV (13, 26). Our center has strict and continuous monitoring at admission and during the stay at the RMU. Another point worth considering is our long use of NIV. Success could be the result of the expertise of our team (physicians and nurses) who have been using NIV for more than 10 years (27).

We are aware that this real-life study has important limitations: 1.It is a single center study and reflects the skills of a single group. Therefore, these data may not be generalized to other settings (28). 2. The effectiveness of any treatment is established by a randomized controlled trial. In the absence of a control group, definitive conclusions cannot be drawn. 3. Microbiological data were available only for a minority of our patients; therefore, different pathogens may have affected patient outcomes. 4. The criteria for intubation were not standardized "a priori" but followed our institutional guidelines. This reflects the "real life"scenario of the study.

CONCLUSIONS

In conclusion, in this observational study, successful treatment was strongly related to less pulmonary involvement and to a prompt and continued response to medical and NIV treatment. Continuous and strict monitoring in an appropriate environment is of paramount importance.

REFERENCES

1. Remington LT, Sligl WI. Community-acquired pneumonia. *Curr Opin Pulm Med* 2014; 20 (3): 215- 24.

2. Carrillo A, Gonzalez-Diaz G, Ferrer M, Martinez-Quintana ME, Lopez-Martinez A, Llamas N, et al. Non-invasive ventilation in community-acquired pneumonia and severe acute respiratory failure. *Intensive Care Med* 2012; 38 (3): 458- 66.
3. Nicolini A, Tonveronachi E, Navalesi P, Antonelli M, Valentini I, Melotti RM, et al. Effectiveness and predictors of success of noninvasive ventilation during H1N1 pandemics: a multicenter study. *Minerva Anestesiol* 2012; 78 (12): 1333- 40.
4. Antonelli M, Conti G, Moro ML, Esquinas A, Gonzalez-Diaz G, Confalonieri M, 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.
5. Carron M, Freo U, Zorzi M, Ori C. Predictors of failure of noninvasive ventilation in patients with severe community-acquired pneumonia. *J Crit Care* 2010; 25 (3): 540.e9-14.
6. Nava S. Behind a mask: tricks, pitfalls, and prejudices for noninvasive ventilation. *Respir Care* 2013; 58 (8): 1367- 76.
7. Timenetsky KT, Aquino SH, Saghabi C, Taniguchi C, Silvia CV, Correa L, Marra AR, Eid RA, Dos Santos OF. High success and low mortality rates with non-invasive ventilation in influenza A H1N1 patients in a tertiary hospital. *BMC Res Notes* 2011; 4: 375.
8. Masclans JR, Pérez M, Almirall J, Lorente L, Marqués A, Socias L, et al. Early non-invasive ventilation treatment for severe influenza pneumonia. *Clin Microbiol Infect* 2013; 19 (3): 249- 56.
9. Cosentini R, Brambilla AM, Aliberti S, Bignamini A, Nava S, Maffei A, et al. Helmet continuous positive airway pressure vs oxygen therapy to improve oxygenation in community-acquired pneumonia: a randomized, controlled trial. *Chest* 2010; 138 (1): 114- 20.
10. Brambilla AM, Aliberti S, Prina E, Nicoli F, Del Forno M, Nava S, et al. Helmet CPAP vs. oxygen therapy in severe hypoxemic respiratory failure due to pneumonia. *Intensive Care Med* 2014; 40 (7): 942- 9.
11. Ferrer M, Cosentini R, Nava S. The use of non-invasive ventilation during acute respiratory failure due to pneumonia. *Eur J Intern Med* 2012; 23 (5): 420- 8.
12. Mas A, Masip J. Noninvasive ventilation in acute respiratory failure. *Int J Chron Obstruct Pulmon Dis* 2014; 9: 837- 52.
13. Santo M., Bonfiglio M,Ferrera L et al.High success and low mortality rates with early use of non invasive ventilation in Influenza A H1N1 pneumonia. *Infect Dis Clin Pract*. 2013; 21(4): 247- 52
14. Schönhofer B, Kuhlen R, Neumann P, Westhoff M, Berndt C, Sitter H. Clinical practice guideline: non-invasive mechanical ventilation as treatment of acute respiratory failure. *Dtsch Arztebl Int* 2008; 105 (24): 424- 33.
15. Díaz GG, Alcaraz AC, Talavera JC, Pérez PJ, Rodriguez AE, Cordoba FG, et al. Noninvasive positive-pressure ventilation to treat hypercapnic coma secondary to respiratory failure. *Chest* 2005; 127 (3): 952- 60.
16. Mandell LA, Wunderink RG, Anzueto A, Bartlett JG, Campbell GD, Dean NC, et al. Infectious Diseases Society of America/American Thoracic Society consensus guidelines on the management of community-acquired pneumonia in adults. *Clin Infect Dis* 2007; 44 Suppl 2: S27- 72.
17. Opravil M, Marincek B, Fuchs WA, Weber R, Speich R, Battegay M, et al. Shortcomings of chest radiography in detecting Pneumocystis carinii pneumonia. *J Acquir Immune Defic Syndr* 1994; 7 (1): 39- 45.
18. Confalonieri M, Potena A, Carbone G, Porta RD, Tolley EA, Umberto Meduri G. Acute respiratory failure in patients with severe community-acquired pneumonia. A prospective randomized evaluation of noninvasive ventilation. *Am J Respir Crit Care Med* 1999; 160 (5 Pt 1): 1585- 91.
19. Erdem H, Turkan H, Cilli A, Karakas A, Karakurt Z, Bilge U, et al. Mortality indicators in community-acquired pneumonia requiring intensive care in Turkey. *Int J Infect Dis* 2013; 17 (9): e768- 72.
20. Ferrer M, Esquinas A, Leon M, Gonzalez G, Alarcon A, Torres A. Noninvasive ventilation in severe hypoxemic respiratory failure: a randomized clinical trial. *Am J Respir Crit Care Med* 2003; 168 (12): 1438- 44.
21. Cilli A, Erdem H, Karakurt Z, Turkan H, Yazicioglu-Mocin O, Adiguzel N, et al. Community-acquired pneumonia in patients with chronic obstructive pulmonary disease requiring

admission to the intensive care unit: risk factors for mortality. *J Crit Care* 2013; 28 (6): 975- 9.

22. Johnson CS, Frei CR, Metersky ML, Anzueto AR, Mortensen EM. Non-invasive mechanical ventilation and mortality in elderly immunocompromised patients hospitalized with pneumonia: a retrospective cohort study. *BMC Pulm Med* 2014; 14: 7.
23. Nicolini A, Ferraioli G, Ferrari-Bravo M, Barlascini C, Santo M, Ferrera L. Early non-invasive ventilation treatment for respiratory failure due to severe community-acquired pneumonia. *Clin Respir J* 2014.
24. Lisboa T, Blot S, Waterer GW, Canalis E, de Mendoza D, Rodriguez A, et al. Radiologic progression of pulmonary infiltrates predicts a worse prognosis in severe community-acquired pneumonia than bacteremia. *Chest* 2009; 135 (1): 165-72.
25. Erdem H, Kocak-Tufan Z, Yilmaz O, Karakurt Z, Cilli A, Turkan H, et al. The interrelations of radiologic findings and mechanical ventilation in community acquired pneumonia patients admitted to the intensive care unit: a multicentre retrospective study. *Ann Clin Microbiol Antimicrob* 2014; 13: 5.
26. Thille AW, Contou D, Fragnoli C, Córdoba-Izquierdo A, Boissier F, Brun-Buisson C. Non-invasive ventilation for acute hypoxemic respiratory failure: intubation rate and risk factors. *Crit Care* 2013; 17 (6): R269.
27. Contou D, Fragnoli C, Córdoba-Izquierdo A, Boissier F, Brun-Buisson C, Thille AW. Noninvasive ventilation for acute hypercapnic respiratory failure: intubation rate in an experienced unit. *Respir Care* 2013; 58 (12): 2045- 52.
28. Carlucci A, Gregoretti C2. Mouthpiece ventilation: just a home-care support? *Respir Care* 2014; 59 (12): 1951- 3.