Risk Factors for Noninvasive Ventilation Failure in Critically Ill Subjects With Confirmed Influenza Infection

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BACKGROUND: Despite wide use of noninvasive ventilation (NIV) in several clinical settings, the beneficial effects of NIV in patients with hypoxemic acute respiratory failure (ARF) due to influenza infection remain controversial. The aim of this study was to identify the profile of patients with risk factors for NIV failure using chi-square automatic interaction detection (CHAID) analysis and to determine whether NIV failure is associated with ICU mortality. METHODS: This work was a secondary analysis from prospective and observational multi-center analysis in critically ill subjects admitted to the ICU with ARF due to influenza infection requiring mechanical ventilation. Three groups of subjects were compared: (1) subjects who received NIV immediately after ICU admission for ARF and then failed (NIV failure group); (2) subjects who received NIV immediately after ICU admission for ARF and then succeeded (NIV success group); and (3) subjects who received invasive mechanical ventilation immediately after ICU admission for ARF (invasive mechanical ventilation group). Profiles of subjects with risk factors for NIV failure were obtained using CHAID analysis. RESULTS: Of 1,898 subjects, 806 underwent NIV, and 56.8% of them failed. Acute Physiology and Chronic Health Evaluation II (APACHE II) score, Sequential Organ Failure Assessment (SOFA) score, infiltrates in chest radiograph, and ICU mortality (38.4% vs 6.3%) were higher ($P < .001$) in the NIV failure than in the NIV success group. SOFA score was the variable most associated with NIV failure, and 2 cutoffs were determined. Subjects with SOFA ≥ 5 had a higher risk of NIV failure (odds ratio = 3.3, 95% CI 2.4–4.5). ICU mortality was higher in subjects with NIV failure (38.4%) compared with invasive mechanical ventilation subjects (31.3%, $P = .018$), and NIV failure was associated with increased ICU mortality (odds ratio = 11.4, 95% CI 6.5–20.1). CONCLUSIONS: An automatic and non-subjective algorithm based on CHAID decision-tree analysis can help to define the profile of patients with different risks of NIV failure, which might be a promising tool to assist in clinical decision making to avoid the possible complications associated with NIV failure. *Key words: influenza infection; CHAID analysis; prognosis; noninvasive ventilation.* [Respir Care 2017;62(10):1307–1315. © 2017 Daedalus Enterprises]

Introduction

Noninvasive mechanical ventilation (NIV) has played a major role in decreasing intubation rates in patients with severe exacerbation of COPD[1-3] and congestive heart failure.[4,5] Despite its wide use in several clinical settings, the

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beneficial effects of NIV in patients with hypoxemic acute respiratory failure (ARF) remain controversial.[6,7] In patients admitted to the ICU for ARF in the context of primary viral pneumonia due to influenza, the intubation rate is particularly high (60%) with reported ICU mortality after intubation of up to 50%.[8-12] Thus, adequate selection of primary viral pneumonia influenza patients with ARF that might benefit from NIV is challenging, because failure may jeopardize their care due to delayed invasive mechanical ventilation. Unsuccessful NIV has been found to be independently associated with increased mortality in subjects with ARF[6,13-18] and warns physicians to adequately select the patient population and monitor closely in order to switch promptly to invasive mechanical ventilation when necessary.

The primary end point of the present study was to identify the profile of patients with early risk factors associated with NIV failure using chi-squared automatic interaction detection (CHAID) analysis with the variables obtained immediately after ICU admission in a large cohort of critically ill subjects with ARF due to influenza infection. The secondary end points were to describe the rate of NIV failure and, finally, to determine whether NIV failure is associated with mortality.

QUICK LOOK

Current knowledge

Recent studies have shown an increase in noninvasive ventilation (NIV) use, both overall and in specific patient populations. Despite its wide use, the beneficial effects of NIV in patients with hypoxemic acute respiratory failure due to influenza infection remain controversial. Unsuccessful NIV has been found to be independently associated with death; however, between 30 and 60% of patients with acute respiratory failure from influenza undergo NIV with a high rate of failure ($>$ 80%). Risk factors for NIV failure and associated mortality are unknown.

What this paper contributes to our knowledge

The NIV failure was frequent (56.8%) among 806 subjects with initial NIV. The ICU mortality was higher (38.4%) than in subjects with initial invasive mechanical ventilation (31.3%). An automatic and non-subjective algorithm based on chi-square automatic interaction detection decision-tree analysis can help to define the profile of subjects with different risks of NIV failure, which might be a promising tool to assist in clinical decision making to avoid the possible complications associated with NIV failure.

Methods

Study Design and Patient Population

This was a secondary analysis of prospective and observational cohorts of critically ill subjects admitted to 148 ICUs in Spain between June 2009 and April 2014.[19-24] Data were obtained from a voluntary registry created by SEMICYUC (Sociedad Española de Medicina Intensiva, Crítica y Unidades Coronarias).

The study was approved by the Joan XXIII University Hospital Ethics Committee (approval 11809). The requirement for informed consent was waived due to the observational nature of the study as reported elsewhere.[19-24]

All consecutive subjects admitted to an ICU for ARF due to influenza viral infection who underwent mechanical ventilation (either invasive or noninvasive) upon ICU admission were included in the study. ICU admission criteria and treatment decisions for all subjects, including the need for NIV or invasive mechanical ventilation, were made according to local standard operating procedures and international guidelines.

NIV was applied to subjects admitted to the ICU who presented an $S_{pO_2} < 90\%$ despite oxygen delivered through

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Supplementary material related to this paper is available at http://www.rcjournal.com.

This study was supported in part by Spanish Society of Critical Care (SEMICYUC) Grant AGAUR 2014/SGR926 and a grant from the Ricardo Barri Casanovas Foundation. The authors have disclosed no conflicts of interest.

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DOI: 10.4187/respcare.05481

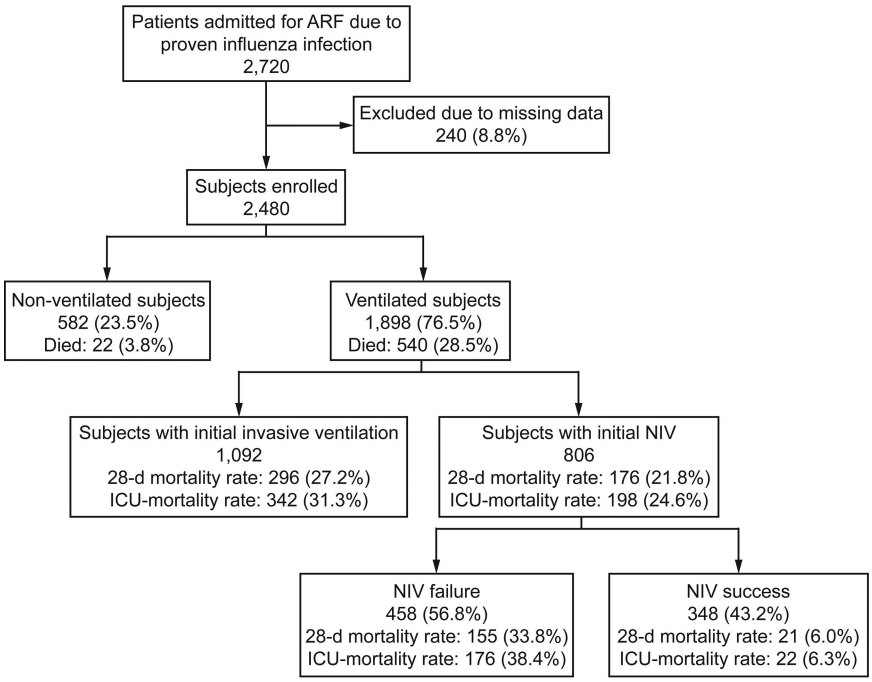

Fig. 1. Flow chart. ARF = acute respiratory failure, NIV = noninvasive ventilation.

a Venturi mask (F_{IO_2} ~0.5) or by oxygen bag (F_{IO_2} ~1). Criteria for endotracheal intubation included failure to maintain an $S_{pO_2} > 90\%$ with a $F_{IO_2} \geq 0.60$, inability to protect the airways or to manage copious tracheal secretions, inability to tolerate the face mask, or progression of respiratory failure defined as sustained hypoxemia despite the increase of the F_{IO_2} or the appearance of hypercapnia.

Patients for whom NIV was used with a do not intubate order were excluded from the study. Patients with missing data were excluded (Fig. 1).

Microbiology

All patients admitted to the ICU with influenza symptoms were systematically tested to confirm influenza A, B, or C infection. Influenza virus infection was confirmed by real-time reverse-transcription polymerase chain reaction in all subjects. The reverse-transcription polymerase chain reaction methods and further details are described elsewhere.[19-24] Only subjects with confirmed influenza infection were included in the study.

Study Groups

Three study groups were considered: (1) subjects who received NIV immediately after admission to the ICU as an initial ventilator support strategy for ARF and then failed (NIV failure group); (2) subjects who received NIV immediately after admission to the ICU as an initial ventilator support strategy for ARF and then succeeded (NIV success group); and (3) subjects who received invasive mechanical ventilation immediately after admission to the ICU as an initial ventilator support strategy for ARF (mechanical ventilation group) (Fig. 1). Study definitions used are shown in the online supplementary material at http://www.rcjournal.com.

Statistical Analysis

Discrete variables are expressed as *n* (%), and continuous variables are expressed as mean ± SD or median (interquartile range). For subjects' demographic and clinical characteristics, differences between groups were assessed using the chi-squared test or Fisher exact test for categorical variables and the Student *t* test or the Mann–Whitney U test for continuous and ordinal variables, when appropriate. Cumulative survival for subjects with and without NIV failure was assessed using the Kaplan–Meier plot. In subjects with NIV, logistic regression analysis was performed to determine which variables were independently associated with NIV failure and mortality. A P value $< .05$ was considered significant.

A CHAID tree is a graphic representation of a series of decision rules. CHAID decision trees are nonparametric procedures that make no assumptions regarding the underlying data.[25-29] Additional information about the CHAID algorithm is shown in the online supplementary material.

Table 1. Characteristics of the 1,898 Subjects Included

Variables	Whole Population (N = 1,898)	Invasive Mechanical Ventilation Group (n = 1,092)	NIV Failure Group (n = 458)	NIV Success Group (n = 348)
Age, median (IQR) y	53 (41–64)	51 (39–62)[a]	53 (42–65)[b]	58 (47–68)[c]
Male sex, *n* (%)	1,139 (60)	643 (58.9)	276 (60.3)	220 (63.2)
APACHE II score, median (IQR)	16 (12–22)	17 (12–23)	17 (13–22)[d]	14 (10–19)[e]
SOFA score, median (IQR)	6 (4–9)	7 (5–10)[f]	7 (4–9)[g]	4 (3–6)[h]
Time between onset symptoms and hospital admission, median (IQR) d	4 (2–6)	4 (2–6)	4 (2–6)	4 (2–5)
Time between onset symptoms and ICU admission, median (IQR) d	1 (1–1)	1 (1–1)	1 (1–1)	1 (1–1)
Quadrants infiltrated in chest radiograph upon ICU admission, median (IQR)	2 (2–4)	3 (2–4)	3 (2–4)[i]	2 (1–3)[j]
Lactate dehydrogenase, median (IQR) U/L	600 (380–970)	625 (383–980)	620 (423–1100)[k]	485 (332–857)[l]
Creatine phosphokinase, median (IQR) U/L	193 (83–500)	214 (94–547)	171 (86–496)	152 (73–364)
Leukocytes $\times 10^9$, median (IQR)	8.1 (4.5–13.0)	8.0 (4.3–13.0)	7.8 (4.3–12.3)[m]	9.1 (5.4–13.6)[n]
Serum creatinine, median (IQR), mg/dL	0.9 (0.7–1.5)	1.0 (0.7–1.5)	0.9 (0.7–1.4)	0.9 (0.6–1.4)
Serum procalcitonin, median (IQR) μg/mL	0.7 (0.2–3.1)	0.9 (0.3–4.1)	0.6 (0.3–2.6)	0.5 (0.2–2.0)
Serum-reactive C-protein, median (IQR) mg/dL	28.7 (14–95)	27.0 (14–87)[o]	31.1 (15–120)[p]	34.2 (14–111)
Comorbidities, *n* (%)				
Asthma	181 (9.6)	86 (7.9)[q]	51 (11.2)[r]	44 (12.6)
COPD	434 (23.0)	211 (19.3)	100 (21.9)[s]	123 (35.2)[t]
Chronic cardiac disease	232 (12.3)	108 (9.9)	53 (11.6)[v]	71 (20.4)[w]
Chronic renal failure	165 (8.7)	83 (7.6)	42 (9.2)	40 (11.5)
Hematologic disease	131 (6.9)	69 (6.3)	37 (8.1)	25 (7.2)
Pregnancy	70 (3.7)	45 (4.1)	14 (3.1)	11 (3.2)
Obesity (body mass index $>$ 30 kg/m^2)	363 (19.2)	208 (19.2)	82 (17.9)	73 (21.0)
Diabetes mellitus	306 (16.1)	146 (13.4)	78 (17.0)[x]	82 (23.6)[y]
Neuromuscular disease	54 (2.9)	32 (2.9)	12 (2.6)	10 (2.9)
Immunodepression (any cause)	217 (11.5)	116 (10.6)	63 (13.3)	40 (11.5)
ICU mortality, *n* (%)	540 (28.5)	342 (31.3)[z]	176 (38.4)[#]	22 (6.3)*

P values are as follows: a vs b, $P = .001$; b vs c, $P = .001$; d vs e, $P < .001$; f vs g, $P = .02$; g vs h, $P < .001$; i vs j, $P < .001$; k vs l, $P = .052$; m vs n, $P = .043$; o vs p, $P = .02$; q vs r, $P = .033$; s vs t, $P < .001$; v vs w, $P < .001$; x vs y, $P = .02$; z vs #, $P = .007$; # vs *, $P < .001$.
NIV = noninvasive ventilation
IQR = interquartile range
APACHE = Acute Physiology and Chronic Health Evaluation
SOFA = Sequential Organ Failure Assessment

In this study, CHAID decision-tree analysis was used to obtain the profile of subjects most strongly associated with NIV failure. NIV failure was the dependent variable, and independent variables at ICU admission were: age, sex, comorbidities, Sequential Organ Failure Assessment (SOFA) score, time between symptom onset and ICU or hospital admission, laboratory testing (hemoglobin, count of leukocytes, serum creatinine, serum urea, lactate dehydrogenase, aspartate aminotransferase, glutamate dehydrogenase, creatine phosphokinase), serum procalcitonin, serum C-reactive protein, number of quadrants with infiltrates on chest radiograph (chest x-ray), and co-infection upon ICU admission. In addition, the predictive accuracy of the model was evaluated by sensitivity, specificity, positive and negative predictive values, and positive or negative likelihood ratio. The statistical analysis with the CHAID method was carried out through the node CHAID included in the SPSS 20.0 statistical program for Windows (IBM, Armonk, New York).

Results

Study Population

A total of 2,720 patients were admitted over a 5-y period. Two hundred forty subjects were excluded due to missing data, and 582 were excluded because they did not receive mechanical ventilation (Fig. 1). The final study population included 1,898 subjects; 1,092 underwent invasive mechanical ventilation, whereas 806 (42.4%) underwent NIV upon ICU admission (Fig. 1). Baseline characteristics of the study population are shown in Table 1.

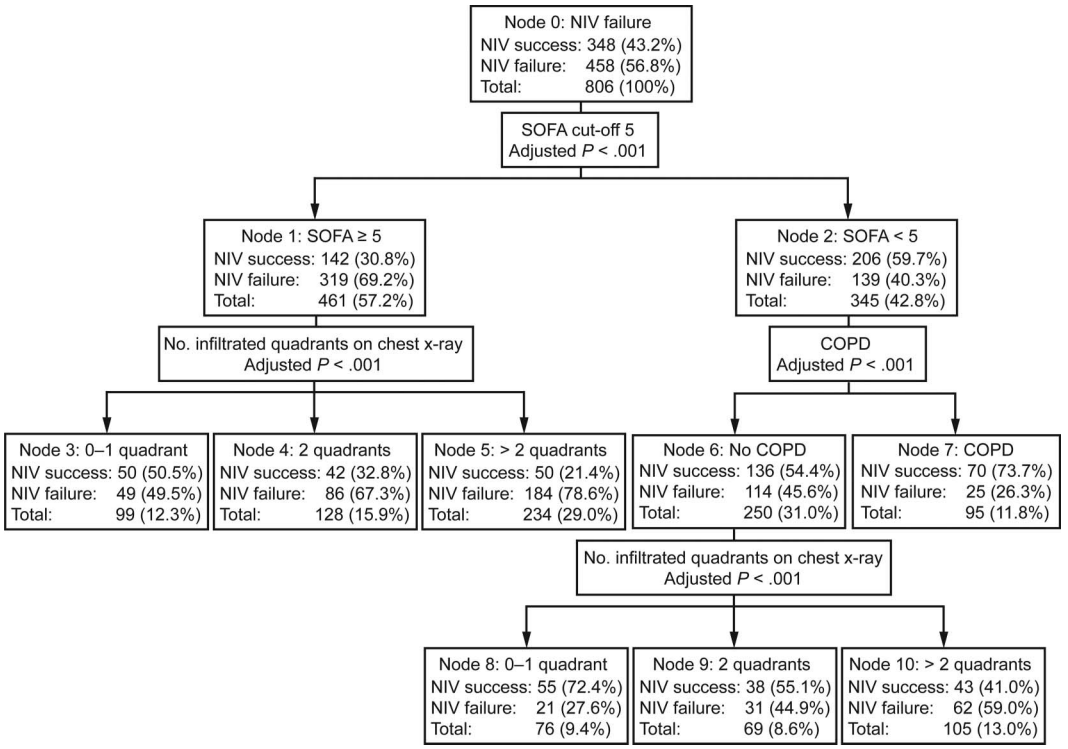

Fig. 2. Tree created by the chi-square automatic interaction detection model for noninvasive mechanical ventilation (NIV) failure. SOFA = sequential organ failure assessment.

Subjects Undergoing NIV Upon ICU Admission

Among the 806 subjects treated with NIV upon ICU admission, NIV failure was reported in 458 subjects (56.8%), and all of them were subsequently intubated and treated with invasive mechanical ventilation. No subjects with NIV failure died before being intubated. The subjects' characteristics are shown in Table 1. Overall, 28-d and ICU mortality rates for subjects undergoing NIV were 21.8% ($n = 176$) and 24.1% ($n = 198$), respectively, with a higher rate in the NIV failure group (33.8 and 38.4%) in comparison with the NIV success group (6.0 and 6.3%, $P < .001$) for 28-d and ICU mortality rates, respectively.

Profile of Subjects With Early Predictors of NIV Failure: CHAID Classification-Tree Analysis

A decision tree with 10 terminal nodes was generated by CHAID analysis (Fig. 2). The gain and index information for each terminal node was summarized in supplemental Table 1. The overall risk estimated was 0.30 with an SE of 0.03, indicating that 70% of the cases will be classified correctly by the decision rules based on the current prediction model. CHAID showed that the severity of multi-organ dysfunction manifested by the SOFA score was the variable most associated with NIV failure upon ICU admission, and 2 cutoffs (< 5 and ≥ 5 points) were generated as the first line of branching. Subjects with SOFA ≥ 5 have a 3-fold risk of failure (OR = 3.3, 95% CI 2.4-4.5, $P < .001$) compared with subjects with SOFA < 5 (Fig. 2) with a post-test probability of 70% for the model. Predictive accuracy of the model should be seen in supplemental Table 2.

Among subjects with a SOFA score < 5 ($n = 345$), NIV failure was 40.3%. In this group, the CHAID tree showed that COPD subjects presented the lowest rates of NIV failure (26.3% vs 45.6%, OR = 2.34, 95% CI 1.3–4.8, $P < .001$) manifested by the strongest association in the second line of branching. Among subjects with a SOFA score < 5 and without COPD, the number of quadrant infiltrates at the chest x-ray was the most important variable in the third line of branching. Among this group of subjects, the presence of infiltrates was associated with a higher possibility of NIV failure (OR = 3.7, 95% CI 1.9–7.5, $P < .001$ for >2 quadrants infiltrated in chest x-ray); see Figure 2.

On the other branch, among subjects with a SOFA score ≥ 5 ($n = 461$), NIV failure was 69.2%. At this partition level, the number of quadrant infiltrates was the most important variable associated with NIV failure in the second line of branching. The NIV failure rate increased significantly ($P < .01$) from 49.5% in subjects without infiltrates to 78.6% in subjects with ≥ 2 quadrants with an OR = 3.75, 95% CI 2.2–6.4, $P < .001$ (Fig. 2).

Table 2. Characteristics of 806 Subjects Who Received Noninvasive Ventilation According to Outcome

Variables	Survivors (n = 608)	Non-survivors (n = 198)	P
Age, median (IQR) y	55 (43–65)	58 (45–72)	.01
Male sex, n (%)	369 (60.7)	127 (64.1)	
APACHE II score, median (IQR)	15.0 (11–19)	19.0 (14–25)	.001
SOFA score, median (IQR)	5 (3–7)	7 (5–10)	.001
Time between onset symptoms and hospital admission, median (IQR) d	4 (2–6)	4 (2–7)	.007
Time between onset symptoms and ICU admission, median (IQR) d	1 (1–2)	2 (1–5)	.001
Quadrants infiltrated in chest radiograph upon ICU admission, median (IQR)	2 (1–3)	3 (1–4)	.001
Lactate dehydrogenase, median (IQR) U/L	560 (358–924)	624 (440–1,100)	
Creatine phosphokinase, median (IQR) U/L	170 (81–490)	140 (65–310)	
Leukocytes $\times 10^9$, median (IQR)	8.5 (5.0–12.8)	7.8 (4.0–13.3)	
Serum creatinine, median (IQR) mg/dL	0.9 (0.7–1.3)	1.1 (0.8–1.8)	
Serum procalcitonin, median (IQR) μg/mL	0.5 (0.2–2.0)	0.9 (0.4–1.20)	
Serum-reactive C-protein, median (IQR) mg/dL	30 (14–114)	37 (17–12.3)	
Comorbidities, n (%)	480 (78.9)	169 (85.4)	
Asthma	78 (12.8)	17 (8.6)	
COPD	172 (28.3)	51 (25.8)	
Chronic cardiac disease	89 (14.6)	35 (17.7)	
Chronic renal failure	50 (8.2)	32 (16.2)	
Hematologic disease	31 (5.1)	31 (15.7)	
Pregnancy	19 (3.1)	6 (3.0)	
Obesity (body mass index $>$ 30 kg/m^2)	124 (20.4)	31 (15.7)	
Diabetes mellitus	116 (19.1)	44 (22.2)	
Neuromuscular disease	18 (3.0)	4 (2.0)	
Immunodepression (any cause)	45 (46.4)	56 (28.3)	.001
NIV failure, n (%)	282 (46.4)	176 (88.9)	.001
Primary viral pneumonia; n (%)	499 (82.1)	178 (89.9)	.006
Community-acquired co-infection, n (%)	102 (16.8)	52 (26.3)	.003
Virus-induced COPD exacerbation	69 (11.3)	7 (3.5)	

IQR = interquartile range
APACHE = Acute Physiology and Chronic Health Evaluation
SOFA = Sequential Organ Failure Assessment
NIV = noninvasive ventilation

We included CHAID-derived variables (SOFA score $\geq$ 5, number of quadrant infiltrates in chest x-ray, and COPD) in a multivariate model to determine their association with NIV failure. SOFA score $\geq$ 5 (OR = 1.22, 95% CI 1.15–1.29, P = .001) and number of quadrants with infiltrates at the chest x-ray (OR = 1.32, 95% CI 1.17–1.49, P = .001) were variables independently associated with NIV failure, and COPD (OR = 95% CI 0.41–0.83, P = .003) was associated with NIV success with a goodness of fit (Hosmer–Lemeshow) for the model of 5.80 (P = .56).

Risk Factors for ICU Mortality in Subjects With NIV

To determine whether NIV failure is associated with ICU mortality, we considered only subjects with NIV. Characteristics of subjects according to outcome are shown in Table 2. A stepwise logistic regression model was performed. As shown in Table 3, age, SOFA score, APACHE II, delayed ICU and hospital admission, immunodepression, primary pneumonia, number of quadrants infiltrated, co-infection, virus-induced COPD exacerbation, and NIV failure were independently associated with increased ICU mortality.

Comparison Between NIV Failure and Invasive Mechanical Ventilation Subjects

The characteristics of 1,092 subjects who underwent invasive mechanical ventilation are presented in Table 1. The 28-d and ICU mortality rates for the invasive mechanical ventilation group (27.2 and 31.3%) were significantly higher than for NIV subjects (21.8 and 24.6%, $P < .001$) but lower than for the NIV failure group (33.8 and 38.4%, P = .01). The adjusted mortality by Cox's (proportional hazards) regression analysis showed higher mortality for the NIV failure group in comparison with the invasive

Table 3. Multiple Logistic Regression Models of Study Variables Associated With ICU Mortality in Subjects With Noninvasive Ventilation

Variable	OR	95% CI	*P*
Age	1.01	1.01–1.03	.030
APACHE II score	1.05	1.03–1.08	<.001
Time between onset symptoms and ICU admission	1.13	1.07–1.19	<.001
No. of quadrants infiltrated in chest radiograph	1.35	1.15–1.58	<.001
No. of comorbidities	1.38	1.15–1.66	<.001
NIV failure	11.45	6.52–20.1	<.001

The goodness-of-fit (Hosmer–Lemeshow) for the model was 3.29 ($P = .92$).
OR = odds ratio
APACHE = Acute Physiology and Chronic Health Evaluation
NIV = noninvasive ventilation

mechanical ventilation group (HR = 1.19, 95% CI 0.99–1.44, $P = .07$); see supplemental Figure 1.

Discussion

The most important finding of our study was that an automatic and non-subjective algorithm based on decision CHAID tree analysis can help to define the profile of subjects with different risks of NIV failure, which might be a promising tool to assist in clinical decision making to avoid the possible complications associated with NIV failure. Another important finding was that NIV failure was frequent in subjects with influenza infection, showing that 1 in 2 subjects who initially received NIV eventually failed with a subsequent 38% ICU mortality. To our knowledge, the present study is the first attempt to generate reasonably simple decision rules to detect the profile of subjects with risks of NIV failure in a large population of ICU subjects by an exhaustive CHAID algorithm of the classification-tree method.

Studies have shown an increase in NIV use, both overall and in specific patient populations.[30-35] However, unsuccessful NIV was found to be independently associated with death, especially in subjects with de novo ARF.[15,16] Following the influenza A (H1N1) pandemic in 2009, several scientific societies considered NIV as a risk factor for the transmission of disease to health-care workers, and its use was discouraged.[36-38] However, between 30 and 60% of patients with ARF from influenza A (H1N1) during the 2009 pandemic were noninvasively ventilated with a high rate of failure (> 80%).[8-12]

Several researchers[8-12] have tried to assess the best predictors of NIV failure in subjects with ARF due to influenza infection. However, these studies have employed standard analysis to detect the risk variables. After applying CHAID analysis, our study showed that the most decisive variable was the SOFA score, followed by COPD and infiltrates at chest x-ray. According to the SOFA CHAID-generated cutoff point, 4 of 10 subjects with SOFA < 5 displayed NIV failure. In this subgroup of subjects, COPD presence was associated with a 50% reduction in of risk failure. Our results are in accordance with previous studies[1-3] that showed that the use of NIV in selected subjects admitted for ARF due to COPD can obviate the need for endotracheal intubation. In contrast, 7 of 10 subjects with SOFA ≥ 5 had NIV failure independently of COPD presence. This allows the hypothesis that once a high level of multi-organ dysfunction is reached, the beneficial effect of NIV for patients with COPD is lost. These findings are consistent with those observed by other authors.[39,40] In contrast, 80% of subjects with SOFA ≥ 5 and the presence of infiltrates in > 2 quadrants required endotracheal intubation, and NIV does not appear to be beneficial in this subset of subjects. Preliminary reports on the use of NIV in subjects with pneumonia and ARF have suggested a consistent association between delayed intubation and increased mortality.[41,42] Although several studies have evaluated the impact of NIV failure in COPD subjects, few studies have assessed its impact on patients with ARF due to influenza infection. Masclans et al[8] observed in 417 subjects a similar ICU mortality rate in subjects who failed NIV (26.5%) and in those who were invasively ventilated from the outset (24.2%, $P = .64$). In our study, NIV failure was associated with an excess of ICU mortality of 7% compared with invasive mechanical ventilation. These contradictory findings could relate to the different power of studies associated with the number of subjects included, 3 times more in our study. Our findings are along the lines of those reported by Brink et al,[11] who observed that 90-d mortality was higher in NIV failure subjects (25%) compared with subjects primarily treated with endotracheal intubation (12%).

The strengths of this study are that it describes the clinical characteristics and outcome of a large series of subjects and applies a novel approach to searching in tools. In addition, our estimation of the prediction model (70%) showed that it was certainly credible, and CHAID analysis could identify the profile of subjects who had a high risk of NIV failure. These patients should receive close monitoring to detect early signs of NIV failure.

However, our study has some limitations that must be acknowledged. First, the observational nature of the study does not allow estimating the cause-effect relationship between the risk factors and outcome, since unmeasured confounding factors may not have been accounted for. Second, no data were recorded on the severity of acute respiratory failure, or blood arterial gases, and no standardized protocol for NIV was used. In addition, these variables are not included in the multivariate analysis of risk factors for NIV failure, although they might reason-

ably play a big role. However, a significant increase in overall use of NIV over time in Spain is consistent with other reports,[33,34] and all ICUs included have highly trained and motivated teams of intensivists and nurses to achieve a high success rate with NIV. Third, in our study the management of NIV, the identification of NIV failure, and the indication for endotracheal intubation were based on the judgment of the attending physician. This variability in the day-to-day ICU medical care decisions is part of real life. Fourth, subjects were recruited only in Spanish ICUs. Therefore, our findings cannot be generalized to other clinical scenarios, such as the emergency department or other countries. Fifth, our study only provides data available at baseline to help determine risk factors for NIV failure, and it does not provide guidance as to when a patient initially given NIV should be intubated. Sixth, we observed that NIV failure was associated with increased mortality in comparison with invasive mechanical ventilation. Time to intubation could be one of the explanations for this observation. However, due to the nature of the database, we do not have data about the time elapsed until the intubation, and we cannot bring clarity to this issue.

Finally, although the CHAID method has great advantages, information overload could occur due to a large quantity of terminal nodes but few patients in each node. In this study, we imposed a very strict model to implement a $P < .05$ and at least restricted to 100 subjects/node, and the resulting final tree can be easily interpreted and applied clinically.

Conclusions

Appropriate patient selection is the key to the successful application of NIV. The selection process takes into account a number of factors, including the patient's severity of illness and risk of failure. Ultimately, it becomes a clinical judgment, depending largely on the physician's experience. In this context, CHAID decision-tree analysis might be a promising tool to identify profiles of patients with a high risk of NIV failure and assist in clinical decision making and avoid complications associated with NIV failure.

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