Prediction of Mortality With the Use of Noninvasive Ventilation for Acute Respiratory Failure

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BACKGROUND: In actuality, it is difficult to obtain an early prognostic stratification for patients with acute respiratory failure treated with noninvasive ventilation (NIV). We tested whether an early evaluation through a predictive scoring system could identify subjects at risk of in-hospital mortality or NIV failure. METHODS: This was a retrospective study, which included all the subjects with acute respiratory failure who required NIV admitted to an emergency department–high-dependence observation unit between January 2014 and December 2017. The HACOR (heart rate, acidosis [by using pH], consciousness [by using the Glasgow coma scale], oxygenation [by using P_{aO2}/F_{IO2}], respiratory rate) score was calculated before the NIV initiation (T0) and after 1 h (T1) and 24 h (T24) of treatment. The primary outcomes were in-hospital mortality and NIV failure, defined as the need for invasive ventilation. RESULTS: The study population included 644 subjects, 463 with hypercapnic respiratory failure and an overall in-hospital mortality of 23%. Thirty-six percent of all the subjects had NIV as the “ceiling” treatment. At all the evaluations, nonsurvivors had a higher mean ± SD HACOR score than did the survivors (T0, 8.2 ± 4.9 vs 6.1 ± 4.0; T1, 6.6 ± 4.8 vs 3.8 ± 3.4; T24, 5.3 ± 4.5 vs 2.0 ± 2.3 [all P < .001]). These data were confirmed after the exclusion of the subjects who underwent NIV as the ceiling treatment (T0, 8.2 ± 4.9 vs 6.1 ± 4.0 [P = .002]; T1, 6.6 ± 4.8 vs 3.8 ± 3.4; T24, 5.3 ± 4.5 vs 2.0 ± 3.2 [all P < .001]). At T24, an HACOR score > 5 (Relative Risk [RR] 2.39, 95% CI 1.60–3.56) was associated with an increased mortality rate, independent of age and the Sequential Organ Failure Assessment score. CONCLUSIONS: Among the subjects treated with NIV for acute respiratory failure, the HACOR score seemed to be a useful tool to identify those at risk of in-hospital mortality. Key words: acute respiratory failure; noninvasive ventilation; prognosis; emergency department; organ failure. [Respir Care 2020;65(12):1847–1856. © 2020 Daedalus Enterprises]

Introduction

Noninvasive ventilation (NIV) has been established as a useful and safe method to improve gas exchange in patients who are critically ill and with acute respiratory failure (ARF) of different etiologies. NIV decreases the work of breathing and improves arterial oxygenation and alveolar ventilation, with a consequent reduction in the use of invasive mechanical ventilation.1–6 In the early 2000s, the main indication was the treatment of exacerbations of COPD and, at the time, NIV reduced the likelihood of endotracheal intubation and in-hospital mortality.7,8 Although the weight of evidence favored a reduction in mortality and endotracheal intubation, further findings that supported NIV
for acute cardiogenic pulmonary edema were not conclusive.\textsuperscript{9,10} Little evidence supports the use of NIV for other causes of ARF, for example, pneumonia.\textsuperscript{11}

Despite the potential harm from the overuse of NIV among patients who are unlikely to benefit from it, the use of NIV has dramatically increased in the past 2 decades in the United States, even in cases that lacked strong supporting evidence.\textsuperscript{12} NIV can be performed outside the ICU and could be a good alternative for patients who are not candidates for invasive mechanical ventilation.\textsuperscript{13} Among such a diverse population, the early identification of patients at increased risk of a poor outcome remains challenging. Duan et al\textsuperscript{14} recently proposed a score for the identification of patients with hypoxemic ARF at high risk of NIV failure. The HACOR (heart rate, acidosis [by using pH], consciousness [by using the Glasgow coma scale], oxygenation [by using $P_{O_2}/F_{O_2}$], respiratory rate) score is based on parameters easily obtainable at bedside. Therefore, it can be repeated after the NIV initiation to monitor the patient’s response to treatment. The present study aimed to test the prognostic value of the HACOR score among the subjects with ARF, treated with NIV in the emergency department.

Methods

Study Design and Setting

This was a retrospective study, performed in the emergency department–high-dependence unit at the Careggi University Hospital. The ethics committee and institutional review board approved this study (13731_oss). The Careggi University Hospital is an urban academic hospital and a tertiary care center (1,300 beds, 130,000 emergency department visits per year). We are accustomed to limited ICU and sub-ICU beds; therefore, between the emergency department and the ICU, we created an area in which patients who are critically ill could be managed and stabilized for 24–48 h to reduce ICU admissions. The emergency department–high-dependence observation unit is a sub-ICU, with equipment for advanced monitoring, NIV, and the possibility to administer vasoactive drugs, managed by emergency physicians. All the subjects were admitted from the emergency department, according to bed availability.\textsuperscript{15} Due to the absence of invasive mechanical ventilators, patients already intubated in the emergency department or those with a high probability of intubation in the first 24 h are admitted directly into the ICU.\textsuperscript{16}

Selection of Participants

All consecutive patients, who were admitted to the emergency department–high-dependence observation unit for respiratory failure in the period January 2014 to December 2017, who were either hypoxemic or hypercapnic, were included in the study. No dedicated respiratory therapist was available in the unit during the study period. The decision to initiate NIV (Philips Respironics Model V680, Respironics, Carlsbad, California) was made by the attending emergency physician based on the guidelines of the American Thoracic Society\textsuperscript{17} and the British Thoracic Society.\textsuperscript{18} Whenever possible, a management plan was made before initiating an NIV trial with regard to what to do in case of failure. The options were to intubate and mechanically ventilate the patient or to consider the NIV trial as a “ceiling” treatment when taking into account the stage of the underlying disease and the wishes of the patient about advanced life support. NIV was initially provided in the emergency department and continued in the emergency department–high-dependence observation unit as soon as a bed became available.

The attending emergency physicians managed the NIV without the presence of respiratory therapists. Pressure support was increased from 5 up to 20 cm H$_2$O to obtain an exhaled tidal volume of 6–8 mL/kg of predicted body weight. The breathing frequency setting was driven by the

Current knowledge

Noninvasive ventilation (NIV) is an established treatment option for patients with an exacerbation of COPD. Among these patients, NIV, in conjunction with usual care, has proved to be beneficial for reducing the likelihood of in-hospital mortality and endotracheal intubation. The HACOR (heart rate, acidosis, consciousness, oxygenation, and respiratory rate) score was recently developed to predict the failure of NIV among patients with hypoxemic respiratory failure: its simplicity and the ability to perform serial evaluations makes it a useful clinical tool.

What this paper contributes to our knowledge

In subjects with hypoxemic or hypercapnic acute respiratory failure, treated with NIV, the HACOR score was significantly higher in those with an adverse outcome. A score $\geq5$ was associated with an increased risk of NIV failure and in-hospital mortality. The trend over the first 24 h added prognostic information to the earliest evaluations, with persistently high values in the subjects with an adverse prognosis. Increasing age and higher degree of organ failure were independent predictors of an unfavorable prognosis among subjects who are critically ill. After adjusting the HACOR score with these 2 parameters, we confirmed the independent association with an increased mortality rate.
attenuation of the activity of respiratory accessory muscles and the achievement of the comfort of the subject (target rate, <30 breaths/min). PEEP was initiated at 5 cm H2O and increased in steps of 2 to 3 cm H2O up to 12 cm H2O, until the FIO2 requirement was ≤0.60 in subjects with hypoxic respiratory failure. Bi-level pressure support was the most commonly used mode of ventilation; CPAP was used for subjects with pulmonary edema without hypercapnia. We defined NIV failure as the need for endotracheal intubation and invasive mechanical ventilation. When adhering to current guidelines, the attending physician decided to intubate the subjects.

**Measurements and Outcomes**

The subjects were identified according to emergency department–high-dependence observation unit admission diagnosis from electronic medical records. For each subject, basic demographic data and previous medical conditions were collected from medical records by using a standardized collection template; the variables needed to construct the score were collected at emergency department admission (T0), after 1 h (T1), and after the first 24 h (T24) from the beginning of NIV. The Sequential Organ Failure Assessment (SOFA) score was calculated at T0 and T24; the APACHE II (Acute Physiology and Chronic Health Evaluation) score was calculated based on the worse values in the first 24 h of staying in the emergency department–high-dependence observation unit. The HACOR score was calculated as indicated in Table 1; it was analyzed as a continuous value and dichotomized as ≤5 or >5, based on the original study. At all the evaluations, the HACOR scores were available in 95% of the whole population; because every subject had one missing HACOR value out of 3, we decided not to delete them from the study. The primary outcomes were in-hospital mortality and NIV failure. NIV failure was evaluated only among patients, who were candidates to invasive mechanical ventilation.

**Statistical Analysis**

Due to the retrospective design of the study, we included all the patients who underwent NIV in the study period. However, based on the reported mortality in the original study (21% in the subjects with a T0 HACOR score ≤5 and 65% in those with a HACOR score >5), the required population size was 60 subjects (power, 95%; α = 5%); we included >600 subjects. Continuous variables were reported as mean ± SD, and comparisons between the 2 groups were performed with the Student t test for unpaired data. Categorical data were analyzed by using contingency tables and the chi-square test. All score comparisons between different groups were performed by using the Mann-Whitney test for nonparametric data. Discrimination ability was tested by building receiver operating characteristic curves and calculating the areas under the curves with 95% CI. Differences in trend among different scores were evaluated by using analysis of variance, we performed a survival analysis by using the Cox logistic regression analysis (input for values <0.05, output for ≥0.10). A P value of <0.05 was considered significant. All statistical analyses were carried out by using SPSS software package, v. 25 (IBM, Armonk, New York).

**Results**

**Characteristics of the Study Participants**

From January 2014 to December 2017, 644 subjects underwent NIV during their emergency department–high-dependence observation unit stay. A total of 181 subjects (28%) had hypoxic ARF, whereas 463 subjects (72%) had hypercapnic ARF. NIV was the ceiling treatment for 223 subjects (35%). The admission diagnoses and the previous medical conditions in our subjects with hypoxic and hypercapnic ARF are shown in Table 2. Compared with the survivors, in both groups, nonsurvivors were older, whereas
the sex distribution was comparable, regardless of prognosis. Among the subjects with hypercapnic ARF, the nonsurvivors had a lower body mass index than did the survivors. Among the most frequent admission diagnoses, COPD exacerbation was more frequent in the subjects with hypercapnic ARF (50% vs 6%; \(P < .001\)). However, pneumonia (62% vs 56%; \(P = .21\)) and cardiac failure (41% vs 34%; \(P = .15\)) showed a similar prevalence in both groups. COPD exacerbation as an admission diagnosis, with a normal chest radiograph, was associated with a lower in-hospital mortality. Sepsis was the admission diagnosis in 19% of our subjects, and it was more frequent among those with hypoxic versus hypercapnic ARF (36% vs 12%; \(P < .001\)) as well as among the nonsurvivors compared with the survivors. The sepsis source was pulmonary in 77% of cases, and in 60 subjects who were septic, NIV was used as the ceiling treatment.

The presence of diabetes among patients with hypoxic ARF and the presence of COPD among those with hypercapnic ARF, were associated with a lower mortality rate. As expected, a significantly higher number of the subjects with hypoxic ARF were treated with CPAP (17% vs 1%; \(P < .001\)) compared with those with hypercapnic ARF. T0 and T24 ventilation pressures were similar in the survivors as well as in the nonsurvivors, both in the subjects with hypoxic and those with hypercapnic ARF (Table 2). The degree of organ failure, expressed by the SOFA score, was more severe in the nonsurvivors than in the survivors.

In Figure 1, we reported the outcome of our subjects according to the ARF etiology and the use of NIV as the ceiling treatment. In the whole study population, in-hospital mortality was 23% and the subjects with hypoxic ARF exhibited a higher mortality versus subjects with hypercapnic ARF (35% vs 19%; \(P < .001\)). This difference was confirmed among the subjects who were candidates for invasive mechanical ventilation in the case of NIV failure (overall mortality rate, 11%, 19% among the subjects with hypoxic ARF, and 9% among those with hypercapnic ARF). The presence of diabetes among patients with hypoxic ARF and the presence of COPD among those with hypercapnic ARF, were associated with a lower mortality rate.

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**Table 2. Clinical Characteristics of the Whole Study Population and Based on the Type of Respiratory Failure**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>All Subjects (N = 644)</th>
<th>Subjects With Hypoxic Respiratory Failure (n = 181)</th>
<th>Subjects With Hypercapnic Respiratory Failure (n = 463)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Survivors (n = 117)</td>
<td>Nonsurvivors (n = 64)</td>
<td>Survivors (n = 377)</td>
</tr>
<tr>
<td>Age, mean ± SD y</td>
<td>78 ± 11</td>
<td>73 ± 14</td>
<td>79 ± 11</td>
</tr>
<tr>
<td>Men, n (%)</td>
<td>332 (52)</td>
<td>48 (41)</td>
<td>23 (36)</td>
</tr>
<tr>
<td>Body mass index, mean ± SD kg/m²</td>
<td>27 ± 7</td>
<td>26 ± 5</td>
<td>24 ± 4</td>
</tr>
<tr>
<td>Admission diagnosis, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>COPD exacerbation</td>
<td>273 (57)</td>
<td>7 (6)</td>
<td>3 (5)</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>371 (58)</td>
<td>72 (62)</td>
<td>40 (63)</td>
</tr>
<tr>
<td>Heart failure</td>
<td>233 (36)</td>
<td>52 (44)</td>
<td>22 (34)</td>
</tr>
<tr>
<td>Sepsis</td>
<td>121 (19)</td>
<td>35 (30)</td>
<td>30 (45)</td>
</tr>
<tr>
<td>Pulmonary embolism</td>
<td>11 (2)</td>
<td>5 (4)</td>
<td>3 (5)</td>
</tr>
<tr>
<td>Chest trauma</td>
<td>19 (3)</td>
<td>5 (4)</td>
<td>0</td>
</tr>
<tr>
<td>NIV parameters</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bi-level modality, n (%)</td>
<td>93 (79)</td>
<td>48 (41)</td>
<td>16 (25)</td>
</tr>
<tr>
<td>T0, mean ± SD</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PEEP</td>
<td>6.6 ± 1.6</td>
<td>6.6 ± 1.5</td>
<td>6.0 ± 1.4</td>
</tr>
<tr>
<td>PS</td>
<td>9.8 ± 3.4</td>
<td>10.6 ± 3.1</td>
<td>12.6 ± 3.6</td>
</tr>
<tr>
<td>T24, mean ± SD</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PEEP</td>
<td>7.1 ± 2.0</td>
<td>7.6 ± 1.8</td>
<td>6.1 ± 1.5</td>
</tr>
<tr>
<td>PS</td>
<td>10.1 ± 4.1</td>
<td>1.9 ± 3.7</td>
<td>12.8 ± 4.1</td>
</tr>
</tbody>
</table>

PMC = previous medical conditions; CAD = coronary artery disease; CKD = chronic kidney disease; NIV = noninvasive ventilation; T0 = emergency department admission; PS = pressure support; T24 = first 24 h from the beginning of NIV
### Table 3. Prognostic Scores in the Subjects With Successful or Failed NIV and in Survivors or Nonsurvivors With Hypoxemic or Hypercapnic ARF, Respectively: NIV Failure

<table>
<thead>
<tr>
<th>Score</th>
<th>Hypoxemic ARF (n = 181)</th>
<th>Hypercapnic ARF (n = 463)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes (n = 22)</td>
<td>No (n = 159)</td>
<td></td>
</tr>
<tr>
<td>SOFA, mean ± SD</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T0</td>
<td>6.0 ± 3.3</td>
<td>5.8 ± 3.4</td>
<td>.70</td>
</tr>
<tr>
<td>T1</td>
<td>6.1 ± 3.0</td>
<td>5.4 ± 3.3</td>
<td>.11</td>
</tr>
<tr>
<td>T24</td>
<td>6.3 ± 3.4</td>
<td>5.2 ± 3.2</td>
<td>.08</td>
</tr>
<tr>
<td>APACHE II, mean ± SD</td>
<td>18 ± 5</td>
<td>18 ± 6</td>
<td>.93</td>
</tr>
<tr>
<td>HACOR, mean ± SD</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T0</td>
<td>7.3 ± 3.4</td>
<td>6.3 ± 4.1</td>
<td>.16</td>
</tr>
<tr>
<td>T1</td>
<td>6.2 ± 3.0</td>
<td>4.7 ± 4.5</td>
<td>.01</td>
</tr>
<tr>
<td>T24</td>
<td>5.5 ± 2.2</td>
<td>4.0 ± 3.6</td>
<td>.02</td>
</tr>
<tr>
<td>HACOR &gt; 5, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T0</td>
<td>(75)</td>
<td>(65)</td>
<td>.52</td>
</tr>
<tr>
<td>T1</td>
<td>(64)</td>
<td>(33)</td>
<td>.02</td>
</tr>
<tr>
<td>T24</td>
<td>(36)</td>
<td>(22)</td>
<td>.07</td>
</tr>
</tbody>
</table>

### Table 4. Prognostic Scores in the Subjects With Successful or Failed NIV and in Survivors or Nonsurvivors With Hypoxemic or Hypercapnic ARF, Respectively: In-Hospital Mortality

<table>
<thead>
<tr>
<th>Score</th>
<th>Hypoxemic ARF (n = 181)</th>
<th>Hypercapnic ARF (n = 463)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes (n = 61)</td>
<td>No (n = 120)</td>
<td></td>
</tr>
<tr>
<td>SOFA, mean ± SD</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T0</td>
<td>7.0 ± 3.5</td>
<td>5.3 ± 3.1</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>T1</td>
<td>6.8 ± 3.4</td>
<td>4.9 ± 2.9</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>T24</td>
<td>6.8 ± 3.6</td>
<td>4.8 ± 2.8</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>APACHE II, mean ± SD</td>
<td>21 ± 6</td>
<td>16 ± 5</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>HACOR, mean ± SD</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T0</td>
<td>8.0 ± 4.9</td>
<td>5.8 ± 3.3</td>
<td>.002</td>
</tr>
<tr>
<td>T1</td>
<td>6.9 ± 5.2</td>
<td>3.9 ± 3.4</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>T24</td>
<td>6.0 ± 4.1</td>
<td>3.3 ± 2.7</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>HACOR &gt; 5, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T0</td>
<td>(79)</td>
<td>(58)</td>
<td>.031</td>
</tr>
<tr>
<td>T1</td>
<td>(30)</td>
<td>(35)</td>
<td>.061</td>
</tr>
<tr>
<td>T24</td>
<td>(34)</td>
<td>(16)</td>
<td>.005</td>
</tr>
</tbody>
</table>

ARF; P = .008) and in subjects with NIV as the ceiling treatment (overall, 44%; 59% vs 37% among the subjects with hypoxemic and hypercapnic ARF; P = .003).

### Predictors of Adverse Outcome

Among the subjects who were candidates for invasive mechanical ventilation (n = 421), NIV failure had occurred in 48 (11% [21% among the subjects with hypoxemic ARF vs 8% among those with hypercapnic ARF]; P = .001). When comparing the subjects successfully treated with NIV versus those who underwent endotracheal intubation, we found that they were of a similar mean ± SD age (73 ± 13 vs 75 ± 12 y P = .32). Among T0 and T1 arterial blood gas parameters, only the mean ± SD P_{O2}/Fi_{O2} was lower with NIV failure (T0, 150 ± 88 mm Hg vs 204 ± 86 mm...
Increased mortality was observed in nonsurvivors compared with survivors in the whole population (T0, 4.9 vs 1.4, P < .001; T1, 4.1 vs 1.8; T24, 4.2 vs 1.8 [all P < .001]), the mean SD HACOR scores were significantly higher in the nonsurvivors than in the survivors. In the whole study population, the discrimination ability evaluated by receiver operating characteristic curves was fair to good, and it improved over the first 24 h (T0, area under the curve 0.64, 95% CI 0.58-0.69; T1, area under the curve 0.68, 95% CI 0.63-0.73; T24, area under the curve 0.75, 95% CI 0.70-0.80 [all P < .001]) (Fig. 3). These data were confirmed in the subjects with hypoxic and hypercapnic ARF (data not shown).

According to the univariate Cox regression analysis, the HACOR score value of >5 was associated with an increased mortality rate at all the evaluations in the whole population and in the subjects with hypercapnic ARF. In those with hypoxic ARF, the association was confirmed at T24 (Table 6). We performed a multivariate Cox regression survival analysis in which we included the dichotomized HACOR score (≤5 or >5), together with the SOFA score and age, which were significantly different between the survivors and nonsurvivors. At T1 and T24, the HACOR score, adjusted by age and the SOFA score, was independently associated with an increased mortality in the subjects with hypercapnic ARF. In the subjects with hypoxic ARF, this result was confirmed only at T24.

We repeated the analysis after the exclusion of the subjects who underwent NIV as the ceiling treatment. In the whole study population (T0, 8.2 ± 4.9 vs 6.1 ± 4.0 [P = .002]; T1, 6.6 ± 4.8 vs 3.8 ± 3.4; T24, 5.3 ± 4.5 vs 2.0 ± 3.2 [all P < .001]) as well as in the subjects with hypoxic ARF (T0, 8.6 ± 4.1 vs 5.8 ± 4.1 [P = .005]; T1, 6.4 ± 4.4 vs 3.3 ± 2.9; T24, 4.2 ± 4.1 vs 1.4 ± 1.8 [all P < .001]), the mean ± SD HACOR scores were significantly higher in the nonsurvivors compared with the survivors. In the whole population and in the subjects with hypercapnic ARF compared with survivors, a significantly higher percentage of the nonsurvivors had a HACOR score of >5 (whole population: T0, 70% vs 50%, T1, 47% vs 23%; T24, 23% vs 8% [P value are as follows: T0, P = .02; T1, P = .001; T24, P = .004]; hypercapnic ARF: T0, 62% vs 45%, P = .17; T1, 48% vs 20% [P = .002]; T24, 20% vs 3% [P < .001]).
Fig. 2. Absolute values and trends of the HACOR (heart rate, aci-
dosis, consciousness, oxygenation, respiratory rate) score during 
the first 24 h based on noninvasive ventilation (NIV) failure (A–C) 
and survival (D–F) in the whole study population (A: within subjects, 
P = .062, between subgroups P = .004; D: within subjects, 
P = .004, and between groups, P < .001), in subjects with hypoxemic ARF (B: 
within subjects, P = .30; between subgroups, P = .02; E: within sub-
jects, P = .20; between survivors and nonsurvivors, P = .001) and 
hypercapnic ARF (C: within subjects, P = .064, between subgroups 
P = .004; F: within subjects P = .067, between survivors and nonsur-
vivors P < .001). The dotted line marks the level of 5, the cutoff value 
suggested by the investigators14 who proposed the score.

Discussion

In a population of subjects admitted to the emergency 
department with ARF, who underwent NIV, we demon-
strated that the HACOR score was significantly higher and 
showed a blunted decrease in the nonsurvivors compared 
with the survivors. In the subjects with hypercapnic ARF, a 
HACOR score > 5 at 1-h and 24-h intervals after the initia-
tion of NIV was independently associated with an increased 
in-hospital mortality. In the subjects with hypoxemic ARF, 
the independent association was confirmed only at T24. In 
the subjects on NIV without limitations to be promoted to 
invasive mechanical ventilation, a HACOR score > 5 was 
associated with a higher rate of endotracheal intubation.

In the past few years, NIV use has increased world-
wide. Despite substantial differences in the evidence that 
supports the use of NIV to treat ARF from COPD or car-
diogenic pulmonary edema compared with other etiolo-
gies, NIV use increased at similar rates, regardless of the 
potential etiology of respiratory failure.12,19 Moreover, 
NIV has been increasingly delivered outside the ICU, in 
the high-dependence observation unit or general ward; 
due to this, the treatment has been used in a higher num-
ber of patients, compared to those admitted to the 
ICU.20,21 Our subjects with ARF, who qualified for invasive 
mechanical ventilation, showed a mortality rate comparable 
with a previous study on subjects treated 
with NIV in high-dependence observation units.22 When 
we considered the whole study population, which 
included a significant proportion of the subjects treated 
with NIV as the ceiling treatment, the mortality rate 
increased. Among candidates for invasive mechanical 
ventilation, the rate of NIV failure was low compared 
with previous studies;23,24,25 this difference could be due 
to the characteristics of our clinical setting, where inva-
sive mechanical ventilation is not feasible. As a result, 
only the subjects at low risk of deterioration in the very 
short-term were admitted to the high-dependence observa-
tion unit.

Most of the previous studies11,12,20 that investigated the 
prognosis of patients treated with NIV focused their attention 
on the incidence and predictors of NIV failure, to identify 
patients early who needed invasive mechanical ventilation as 
the final treatment. All the investigators agree to identify 
NIV failure and delayed endotracheal intubation as predic-
tors of an increased in-hospital mortality. However, for a 
“real world” study population like this, it is of utmost impor-
tance to find a feasible tool for the early identification of 
patients at high risk of an adverse prognosis. Previous stud-
ies26,27 did not find reliable parameters to stratify the risk of 
death. Fiorino et al26 in a population of patients with hyper-
capnic respiratory failure managed in an experienced general 
ward found that an increased age and a depressed Glasgow 
coma scale score were associated with an adverse prognosis. 
A higher APACHE score proved to be associated with a 
higher mortality rate.27 However, the ability to predict NIV 
failure is low when based only on a single variable.

The HACOR score was recently developed by Duan et 
al,14 for the prediction of NIV failure in patients with hypo-
xemic respiratory failure. The scale takes into account heart
rate, acidosis, consciousness, oxygenation, and respiratory rate, variables that can be obtained by simple bedside measurements. Thus, the HACOR score is a feasible tool to assess baseline conditions and the patients’ evolution over time because it can be easily repeated at short intervals. We decided to test the accuracy of the scale in predicting inhospital mortality. The possibility to perform serial evaluations; the inclusion of parameters, which were significantly different between the survivors and nonsurvivors in hypoxemic and hypercapnic ARF; and the easy calculation of the score motivated our choice. The score demonstrated a fair-to-good prognostic accuracy; however, a value of the HACOR score of >5 according to the cutoff proposed in the original study, proved to be independently associated with a higher mortality, after the adjustment for age and severity of co-existing organ damage.
Before starting the treatment with NIV, the survivors and the nonsurvivors had shown similar values of the HACOR score, as if parameters collected before the initiation of NIV did not allow the subjects with an adverse prognosis. However, the 1- and 24-h values discriminated between the subjects with a good or an unfavorable prognosis because the early positive response to the treatment with NIV exerted a significant effect on the outcome. In fact, the trend over the first 24 h added prognostic information to the earliest evaluations. The persistence of high values during this period was associated with an increased risk of NIV failure or inhospital mortality. To the best of our knowledge, for the first time, a feasible score was tested in a large “real-world” clinical setting could limit the applicability of our results, especially outside of European countries, where this type of emergency department organization is uncommon. A significant proportion of our study population underwent NIV as the ceiling treatment and, from a certain point of view, this can be considered a major limitation. Due to this, we added data about the prognostic value of the HACOR score after the exclusion of the subjects who underwent NIV as the ceiling treatment. However, our study population represented the patients who undergo NIV in everyday clinical practice. With our subjects, we were able to test the prognostic tool to give clinicians useful information for the early identification of those at high risk of an adverse outcome.

### Conclusions

Among the subjects treated with NIV for hypoxemic or hypercapnic ARF, the HACOR score proved to be a useful and feasible tool for an early identification of those at risk of an adverse prognosis. The evolution of the score over the first 24 h added prognostic information to the earliest evaluations. The persistence of high values during this period was associated with an increased risk of NIV failure and in-hospital mortality. The easy calculations at bedside make this score a promising tool for the prognostic
stratification of subjects treated with NIV because it allows the early identification of those at high risk of an adverse outcome.

REFERENCES