Evolution of Patients With Chronic Obstructive Pulmonary Disease, Obesity Hypoventilation Syndrome, or Congestive Heart Failure Undergoing Noninvasive Ventilation in a Respiratory Monitoring Unit

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OBJECTIVE: We compared the use of noninvasive ventilation (NIV) for hypercanic acidosis with hypoxemia in patients with chronic obstructive pulmonary disease (COPD), obesity hypoventilation syndrome (OHS), or congestive heart failure (CHF) in a respiratory medicine monitoring unit. The objective was to evaluate each diagnostic group’s response to therapy in terms of clinical course and evolution of blood gases.

PATIENTS AND METHODS: Prospective, 12-month study of 53 patients with hypercanic acidosis with hypoxemia. Twenty-seven patients had COPD, 17 OHS, and 9 CHF. Severity was assessed based on initial arterial blood gas analysis. Clinical course was studied by blood gas analysis after conventional treatment and after NIV (1-3 hours and 12-24 hours). Mortality was recorded. All patients received bilevel positive airway pressure support in assist-control mode.

RESULTS: No significant differences were observed between mean (SD) initial pH findings in the 3 diagnostic groups: COPD, 7.28 (0.1); OHS, 7.29 (0.09); and CHF, 7.24 (0.07). (nonsignificant differences). After initial conventional treatment, PaCO₂ worsened for COPD patients (P = 0.026) and PaO₂ improved for CHF patients (P = 0.028). After 1 to 3 hours of NIV, pH (P = 0.002) and PaO₂ (P = 0.041) improved for COPD patients, and pH (P = 0.03) and PaCO₂ (P = 0.045) improved in OHS patients; no significant changes were observed in CHF patients. After 12 to 24 hours of NIV, the mean pH was 7.36 (0.04) for COPD patients, 7.36 (0.05) for OHS patients, and 7.25 (0.1) for CHF patients (not significant). The morality rate was 11.1% for COPD, 0% for OHS, and 33.3% for CHS (not significant, P = 0.076).

CONCLUSIONS: In this group of patients with similar initial arterial blood gas values, response to NIV was seen to be better in OHS and COPD than in CHF. That the start of NIV is usually preceded by a poor response to conventional COPD treatment suggests that delaying NIV should be reconsidered.


Evolución comparativa con ventilación no invasiva de pacientes con EPOC, síndrome de hipoventilación-obesidad e insuficiencia cardíaca congestiva ingresados en una unidad de monitorización respiratoria

OBJETIVO: Hemos realizado un trabajo comparativo en pacientes con enfermedad pulmonar obstructiva crónica (EPOC), síndrome de hipoventilación-obesidad (SHO) e insuficiencia cardiaca congestiva (ICC) sometidos a ventilación no invasiva (VNI) en una unidad de monitorización de neumología por presentar acidosis hipoxémica-hipercápncia. El objetivo ha sido valorar la respuesta clínica y gasométrica en función del diagnóstico.

PACIENTES Y MÉTODOS: Se trata de un estudio prospectivo (12 meses de duración) en 53 pacientes con acidosis hipoxémica-hipercápncia, de los que 27 presentaban EPOC; 17, SHO, y 9, ICC. Realizamos un análisis de la gravedad gasométrica inicial, de la evolución gasométrica (tras tratamiento convencional y tras VNI a las 1-3 h y 12-24 h) y de la mortalidad. Todos ellos recibieron VNI tipo BiPAP en modo asistido-controlado.

RESULTADOS: La presentación gasométrica inicial era similar en las 3 entidades (valores medios ± desviación estándar de pH, 7,28 ± 0,1 en la EPOC; 7,29 ± 0,09 en SHO, y 7,24 ± 0,07 en ICC; no significativo). Tras tratamiento convencional inicial, en los pacientes con EPOC se observó un empeoramiento de la presión arterial de anhídrido carbónico (p = 0,026), y en aquellos con ICC, una mejoría de la presión arterial de oxígeno (p = 0,028). Tras el inicio de la VNI (1-3 h) se produjo una mejora del pH (p = 0,002) y de la presión arterial de oxígeno (p = 0,041) en la EPOC, y del pH (p = 0,03) y de la presión arterial de anhídrido carbónico (p = 0,045) en el SHO; no hubo cambios significativos en la ICC. Tras 12-24 h con VNI, el pH fue de 7,36 ± 0,04 en la EPOC, de 7,36 ± 0,05 en el SHO y de 7,25 ± 0,1 (no significativo) en la ICC. La mortalidad fue del 11,1% en la EPOC, del 0% en el SHO y del 33,3% en la ICC (no significativo; p = 0,076).

CONCLUSIONES: Partiendo de una gravedad gasométrica similar, en el SHO y la EPOC se observó una mejor respuesta a la VNI que en la ICC. El inicio de la VNI suele precederse de mala respuesta al tratamiento convencional en la EPOC, lo que haría replantearse la demora para iniciarla.
Introduction

The use of positive airway pressure for noninvasive ventilation (NIV) has gradually spread from its traditional clinical setting in patients with chronic respiratory failure to include acute respiratory failure from any cause. The earliest experiences with positive airway pressure NIV for acute respiratory failure were reported in 1989 and 1990.\(^1\) In this context, several studies have demonstrated that NIV is effective both in partial respiratory insufficiency and in hypercapnic acidosis with hypoxemia, and it is in exacerbations of chronic obstructive pulmonary disease (COPD) where the greatest weight of evidence has accumulated. In both COPD and in the presence of hypercapnic acidosis with hypoxemia, NIV has proven able to reduce both mortality and the requirement for orotracheal intubation and to shorten the average hospital stay.\(^2\) NIV has proven useful not only in intensive care units (ICUs) but also on conventional wards.\(^3-5\) Plant et al\(^6\) carried out a multicenter study of 236 patients with exacerbated COPD admitted to conventional respiratory medicine wards. NIV rapidly reduced respiratory acidosis in treated patients in comparison with controls; both mortality and the need for orotracheal intubation also decreased. These findings were confirmed by a recent meta-analysis by Fernández Guerra et al.\(^6\)

The application of NIV in acute respiratory failure and hypercapnic acidosis with hypoxemia extends to other settings: acute pulmonary edema, immune system compromise, ventilator weaning, asthma, pneumonia, cystic fibrosis, or postoperative recovery.\(^7\) NIV has also proven useful on conventional hospital wards in patients with severe hypercapnic encephalopathy who are ineligible for ICU admission and who need only basic monitoring.\(^8\) A recent review by Liesching et al\(^9\) analyzed the evidence supporting the use of NIV for acute respiratory failure in different disease contexts. The reviewers found strong evidence supporting the use of NIV in COPD exacerbation and acute pulmonary edema (stronger in the latter for continuous positive airway pressure), whereas the evidence base for NIV in obesity hypoventilation syndrome (OHS) was weaker. Only observational studies have been done for OHS.\(^10\) Several studies have also demonstrated that NIV is cost effective in some of these disease settings. Another British study led by Plant et al\(^11\) (14 hospitals, 236 patients) showed NIV to be highly cost effective as well as able to reduce mortality in patients treated on conventional wards for exacerbated COPD and mild to moderate acidosis.

We present a comparative study of patients with 3 diagnoses—COPD, OHS and congestive heart failure (CHF)—who received NIV for hypercapnic acidosis with hypoxemia in a respiratory monitoring unit for patients under the supervision of the pneumology department. The aims were to evaluate NIV use and prognosis in each disease context, determining baseline status, the response to initial conventional treatment, and evolution of blood gas parameters and clinical picture after initiation of NIV.

Patients and Methods

This prospective, observational study from November 2003 to November 2004 included all patients admitted to our hospital’s respiratory monitoring unit with acute respiratory failure and hypercapnic acidosis with hypoxemia (n=88). All had been admitted by the emergency department; after assessment by the ICU staff and once admission to that unit had been ruled out, our group proceeded to evaluate initial tolerance to NIV. Treatment was started for all patients considered candidates for management in the respiratory monitoring unit and not requiring ICU admission. Patients eligible for respiratory monitoring unit care had hypercapnic acidosis, with a pH of 7.25 or higher, hypoxemia, and no concomitant disease; their initial tolerance of NIV was good. Criteria indicating that intensive care was needed were severe acidosis (pH<7.25), multiple organ failure, NIV intolerance, and a prior clinical status that would justify ICU care. These criteria also led to admission to the respiratory monitoring unit of a group of patients with severe hypercapnic acidosis, pH<7.25, hypoxemia, and comorbidity but who were not candidates for ICU admission because of their prior clinical status. We analyzed the evolution of arterial blood parameters from before admission (while the patient was still in the emergency department) and upon admission in 3 of the 4 most prevalent diseases present in our respiratory monitoring unit (COPD, OHS, and CHF), observing the response to NIV in terms of arterial blood parameters and symptoms. Most of the patients with CHF had signs indicative of a diagnosis of acute cardiogenic pulmonary edema. The respiratory monitoring unit had 3 beds and a staff pneumologist available on the morning shift, with or without a resident doctor. General internal medicine specialists or pneumology residents without specific assignment to the unit covered the other shifts. When physicians from the pneumology department were unavailable for afternoon, night or weekend duty, precise instructions were left for each patient, following departmental procedures. For new admissions, the physician on duty for afternoon, night, or weekend shifts was to consult the ICU staff. Nurses maintained visual contact with the monitoring unit from the nursing station, which is also equipped with centralized monitoring equipment.

Patients were excluded if they were eligible for ICU admission (quality of life, underlying disease, etc)\(^12\) and if there were clinical or radiologic signs of pneumonia, a diagnosis that was considered apart. Variables recorded were pH, PaO\(_2\), and PaCO\(_2\). Conventional treatment consisted of systemic glucocorticoids and furosemide, and antibiotics as appropriate. The NIV technique used was bilevel positive airway pressure support with a Quantum series 7700 respirator (Respironics, Atlanta, Georgia, USA) and a Respironics face mask.
ORTEGA GONZÁLEZ A ET AL. EVOLUTION OF PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE, OBESITY HYPOVENTILATION SYNDROME, OR CONGESTIVE HEART FAILURE UNDERGOING NONINVASIVE VENTILATION IN A RESPIRATORY MONITORING UNIT

Results

COPD was the diagnosis for 27 (30.7%), of the 88 patients treated in the respiratory monitoring unit in the study period (46 men and 42 women, mean [SD] age 72.9 [10.9] years; 17 (19.3%) had OHS, and 9 (10.2%) had CHF. Eleven patients (12.5%) with pneumonia were excluded from the analysis for the association of pneumonia with other diseases; other exclusions were 5 (5.7%) with kyphoscoliosis or other restrictive diseases, because their number was small, and 19 (21.6%) with other diagnoses or conditions overlapping the aforementioned ones. Table 1, which gives the characteristics of the 88 patients admitted, shows that the mean length of hospital stay was 4.5 (4.6) days overall, with no significant differences by diagnosis. The settings were tailored for each patient, with an inspiratory pressure between 12 and 18 cm H2O and an expiratory pressure between 4 and 8 cm H2O. The inspiratory pressure ramp ranged from 0.4 to 0.6 seconds and the inspiratory to expiratory time ratios and respiratory frequency were also tailored. NIV was continuous until pH became normal. Then it was used in sessions several hours long during nursing shifts; later it was stopped completely after pH and PaCO2 were both normal or when only pH was normal with hypercapnia holding steady for at least 48 hours. At that point the patient was discharged from the monitoring unit and transferred to a conventional pneumology ward or home.

Other variables analyzed were mortality overall and by diagnosis in the respiratory monitoring unit, mean length of stay in the unit overall and by diagnosis, and number of hours required for pH to become normal by diagnosis for those patients who achieved that goal. Patients’ respiratory function status before hospitalization was also analyzed in terms of the 3 aforementioned diagnostic groups.

Statistical Analysis

SPSS software was used for statistical analysis. Differences between groups for each variable were analyzed with the Wilcoxon signed rank test and the χ2 test. Statistical significance was set at a level of P less than .05.

Table 2 shows the lung function status of the 53 patients assessed in stable condition. Figure 1 shows the prevalence of each diagnosis during the study period.

The initial arterial blood parameters, and therefore severity based on those values, were similar in the 3 diagnostic groups, as there were no statistically significant differences in pH, PaO2, or PaCO2. Thus, the initial pH ranged from 7.24 in the CHF group to 7.29 in the OHS group; the mean initial PaO2 ranged from 55 to 61 mm Hg in the 3 diagnostic groups, and PaCO2 ranged from 61 to 67 mm Hg.

After conventional treatment (mainly in the emergency department) hypercapnia worsened in spite of an increase in PaO2 in all 3 groups (significant in the CHF group, to

**Table 1**

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>FEV1, %</th>
<th>FVC, %</th>
<th>FEV1/FVC, %</th>
<th>PaO2, mm Hg</th>
<th>PaCO2, mm Hg</th>
</tr>
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<tbody>
<tr>
<td>COPD</td>
<td>35.06</td>
<td>62.62</td>
<td>41.86</td>
<td>49.94</td>
<td>48.22</td>
</tr>
<tr>
<td>OHS</td>
<td>68.02</td>
<td>70.09</td>
<td>78.02</td>
<td>58.75</td>
<td>50.09</td>
</tr>
<tr>
<td>CHF</td>
<td>69.6</td>
<td>78.5</td>
<td>70.83</td>
<td>56.33</td>
<td>52.38</td>
</tr>
</tbody>
</table>

COPD indicates chronic obstructive pulmonary disease; OHS, obesity hypoventilation syndrome; CHF, congestive heart failure.

**Figure 1.** Prevalence of 3 diagnoses in the population of patients treated in the respiratory monitoring unit. COPD indicates chronic obstructive pulmonary disease; OHS, obesity hypoventilation syndrome; CHF, congestive heart failure.

**Table 2**

*Data are expressed as mean (SD) unless otherwise indicated. COPD indicates chronic obstructive pulmonary disease; OHS, obesity hypoventilation syndrome; CHF, congestive heart failure.*

**Table 1**

<table>
<thead>
<tr>
<th>Patient Characteristics (n=88)*</th>
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<tbody>
<tr>
<td>Age, mean, y</td>
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<tr>
<td>Sex</td>
</tr>
<tr>
<td>Men</td>
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<tr>
<td>Women</td>
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<tr>
<td>Hospital stay, mean, d</td>
</tr>
<tr>
<td>Overall</td>
</tr>
<tr>
<td>COPD</td>
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<tr>
<td>OHS</td>
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<tr>
<td>CHF</td>
</tr>
<tr>
<td>NIV, time until normal pH, h†</td>
</tr>
<tr>
<td>COPD</td>
</tr>
<tr>
<td>OHS</td>
</tr>
<tr>
<td>CHF</td>
</tr>
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*For patients who achieved a normal pH.
69.37 mm Hg, \(P=0.028\)). PaCO\(_2\) rose significantly in the COPD group, to 70.09 mm Hg \((P=0.026)\). There was no normalization of pH in any group.

Comparison of arterial blood parameters before and 1 to 3 hours after start of NIV showed a significant improvement in pH in the COPD \((P=0.002)\) and OHS \((P=0.03)\) groups and a tendency toward improvement in the CHF group. PaO\(_2\) also improved in the COPD group \((P=0.041)\), but the other diagnostic groups saw no significant changes. Similarly, PaCO\(_2\) tended to improve in the COPD and CHF groups but the change was significant only in the OHS group \((P=0.045)\).

At 12 to 24 hours of NIV, mean pH levels were normal in the COPD \((7.36 \pm 0.04)\) and OHS \((7.36 \pm 0.05)\) groups but acidosis was still present in the CHF group at 7.25 \((0.1)\). However, pH differences between the groups were not significant. PaCO\(_2\) levels tended toward normal in the COPD and OHS groups, but not in the CHF group.

Figures 2 through 4 show the evolution of pH, PaO\(_2\), and PaCO\(_2\) values by diagnosis in function of hours of NIV treatment. Table 1 shows the number of hours required to normalize pH within each diagnostic group (for patients who achieved that goal).

Overall mortality for all 88 patients treated in the respiratory medicine monitoring unit was 15.9%. Considering the 53 patients in the 3 diagnostic groups analyzed, mortality was 11.1% in the COPD group, 0% in the OHS group, and 33.3% in the CHF group. In spite of the magnitude of the differences observed, they were not statistically significant \((P=0.076)\). Figure 5 depicts mortality overall and by diagnosis.
Discussion

This study suggests that NIV may be more effective for acute respiratory failure with hypercapnic acidosis and hypoxemia in the context of OHS and COPD than in patients with CHF. In this sense, the absence of differences in arterial blood parameters between patients undergoing NIV for the 3 diagnoses analyzed confirmed that initial severity was similar and allowed differences in clinical course to be distinguished. The greater efficacy of NIV is not only demonstrated by changes in arterial blood parameters. The trend in mortality rates is also consistent with the hypothesis of differences in clinical course. We found no other studies in the literature in which similar comparisons were made within a pneumology department. However, there are a number of ICU studies comparing the efficacy of NIV in terms of the course of arterial blood parameters, mortality, and other clinical variables in the context of specific diseases; a few such studies have been done in the setting of conventional wards. Robino et al. established that NIV was more effective in correcting hypercapnic acidosis with hypoxemia in restrictive diseases than in obstructive ones, analyzing data from arterial blood analysis and clinical parameters. Patients with kyphosis, scoliosis, or other restrictive chest disorders were not included because their numbers were very low (n=5).

The initial arterial blood gas analyses for our series, usually performed in the emergency department, showed moderate acidosis with mean pH levels ranging from 7.24 to 7.29, depending on disease. Acidosis in the COPD group (mean pH, 7.28) was more similar to that of ICU patients on NIV who have been studied.6

The efficacy of conventional treatment before NIV varied. A significant improvement in PaO2 was achieved only in the CHF group with conventional treatment, although there was a general trend toward improvement in the other groups. However, arterial blood analysis revealed a generally poor response to that treatment in terms of acidosis in comparison with the initial situation. That poor response to conventional treatment was most significant in the COPD group, calling its application there into question and suggesting that NIV should be started earlier in this setting.

Our findings suggest clear conclusions with regard to OHS. The overall prognosis for NIV treatment of acute respiratory failure in this setting is excellent. The absence of deaths was a remarkable observation; other reports in the literature are not consistent with this finding. Only observational data are available and it would be useful to design studies with larger samples of patients. The improvement in parameters derived from arterial blood analysis was especially positive at the first check (between 1 and 3 hours after starting NIV). After that, all parameters tended to improve steadily toward normalization until the 24-hour analysis. This first 24-hour trend toward improvement was slower for PaO2 and PaCO2 than for pH.

Overall, clinical course after the use of NIV was favorable in the COPD group at 24 hours, with normalization of pH. There is a large body of literature reporting clinical course and mortality rates for this disease in the context of pneumology departments and ICUs. In our COPD and OHS patients, NIV was particularly effective in the first 3 hours, improving pH; moreover, PaO2 improved more for COPD patients than for other groups. Del Castillo et al.4,11 analyzed the different evolution of 41 patients with COPD and hypercapnic acidosis and hypoxemia who were randomly assigned to receive conventional medical treatment or NIV on a conventional ward. The improvement in pH was significantly greater for the patients receiving NIV in comparison with the controls after 2 hours of treatment. PaO2 also improved after the second hour, but the differences between the NIV and conventional therapy groups were not significant. Other similar studies, however, have reported significant improvement in PaO2.14,15 Regarding the improvement in hypercapnia in COPD, our findings were consistent with others’ who observed that PaCO2 underwent a slower progression to normal; the decrease in PaCO2 became more evident after 6 hours in the study of González Barcala et al.13 and after 12 hours in other studies.4,16 Mortality in our series for COPD, at 11.1%, was closer to that observed in ICUs than on respiratory medicine wards. In a meta-analysis concerned with the efficacy of NIV in COPD exacerbations, Fernández Guerra et al.6 found that the overall mortality on internal medicine wards was 9.7%, ranging from 5.8% to 10.2%. In ICUs mortality was 10.7% overall and ranged from 8.3% to 13.8%. This can be explained partly because our patients had a level of initial acidosis (pH, 7.28 [0.1]) that was quite similar to that reported for ICU series and clearly different from the acidosis found in conventional ward patients, as we have pointed out. Mortality was 8.5% in a series described by González Barcala et al.13 Their patients had an initial pH of 7.29 on the average, higher than the mean pH we observed, and the initial PaCO2 in their series was 75.4 mm Hg, also somewhat higher than in ours. We do not know whether these patients would have had a better outcome if admitted to the ICU. Given that such admission was ruled out based on the aforementioned criteria, the possibility of offering monitored NIV treatment was a reasonable choice among the alternatives of usual clinical practice.

With respect to the worse course of blood gas parameters and clinical picture in CHF patients (mean pH levels failed to become normal within 24 hours and mortality was 33%), other studies in the literature, mainly carried out in ICUs, have reported very similar findings, supporting the hypothesis that NIV is less useful in CHF.17 Thus, Rodríguez Mulero et al.18 studied 199 patients with acute pulmonary edema and respiratory failure admitted to an ICU, where they were treated with bilevel positive airway pressure in 93% of the cases: the mortality rate they reported was 32.7%. Patient age in that study was similar to our patients’ and acidosis and hypercapnia were less severe, based on findings of arterial blood analysis before NIV: pH, 7.27 versus 7.22 in our study and theirs, respectively, and
PaCO$_2$, 56.5 mm Hg versus 77.8 mm Hg. Similarly, Vailipour et al. reported a mortality rate of 28.5% in a study of 28 patients. Our patients only achieved improved pH and PaCO$_2$ after the start of NIV (analysis at 1 to 3 hours), although the trend was not statistically significant and was not maintained in subsequent arterial blood analyses. Furthermore, a worsening of PaO$_2$ was observed, breaking the positive trend after conventional treatment, although the change was not significant. Both pH and PaCO$_2$ improved significantly within the first hour of NIV treatment for the patients of Rodríguez Mulero et al. 38

Two factors, however, may have contributed to the poor clinical course we observed in CHF patients. First, such patients admitted to our unit with hypercapnic acidosis and hypoxemia were not considered ICU candidates because of their age, quality of life, or comorbidity. This would explain why they were initially in more serious condition than the other 2 diagnostic groups analyzed. Second, this group probably had a higher rate of comorbidity.

The relevance of comorbidity was pointed out by Scala et al., who analyzed the impact of nonrespiratory comorbidity on the short-term prognosis for exacerbated COPD patients with acute respiratory failure treated in a monitoring unit similar to ours. The prevalence of NIV failure was higher in that series of 120 patients when such comorbidity was present. The rate of acute nonrespiratory comorbidity (mainly cardiovascular disease) was 41.7%.

Some authors have demonstrated that the improvement in pH and the reduction of respiratory frequency in the first hour were, as is logical, the indicators that define the success of NIV in patients with acute respiratory frequency. Some of those studies have also found that hypercapnia without an important degree of associated hypoxemia is a better indicator for this treatment than severe hypoxemia alone. In addition to comorbidity, it would have been interesting to analyze other factors that might be associated with mortality in these patients. Raurich et al. found that hospital mortality was related to age over 65 years, presence of chronic cor pulmonale and certain complications such as cardiac arrest before starting ventilation, ventricular and atrial arrhythmias during ventilation, and multiorgan dysfunction syndrome in a study of COPD patients in an ICU.

In summary, bilevel positive airway pressure NIV was more efficacious in OHS and COPD than in CHF in patients with similar initial severity reflected by arterial blood parameters. The initial conventional treatment did not reverse respiratory acidosis in any of the diseases analyzed, and response to such treatment was significantly less satisfactory in COPD patients. In these circumstances, and for COPD patients, the practice of delaying the start of NIV therapy in moderate or severe hypercapnic acidosis with hypoxemia should be reconsidered. NIV should be implemented based on the initial arterial blood gas analysis. Finally, some studies suggest that intermediate care units, including respiratory monitoring units, are the ideal cost-effective solution for care between the ICU and conventional wards. Results reported by units like ours should serve to make intermediate and respiratory monitoring units more widely accepted, as they are still scarce in Europe and even scarcer in Spain.

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