Non-invasive ventilation after extubation in hypercapnic patients with chronic respiratory disorders: randomised controlled trial

Miquel Ferrer, Jacobo Sellarés, Mauricio Valencia, Andres Carrillo, Gumersindo Gonzalez, Joan Ramon Badia, Josep Maria Nicolas, Antoni Torres

Summary

Background Non-invasive ventilation can prevent respiratory failure after extubation in individuals at increased risk of this complication, and enhanced survival in patients with hypercapnia has been recorded. We aimed to assess prospectively the effectiveness of non-invasive ventilation after extubation in patients with hypercapnia and as rescue therapy when respiratory failure develops.

Methods We undertook a randomised controlled trial in three intensive-care units in Spain. We enrolled 106 mechanically ventilated patients with chronic respiratory disorders and hypercapnia after a successful spontaneous breathing trial. We randomly allocated participants by computer to receive after extubation either non-invasive ventilation for 24 h (n=54) or conventional oxygen treatment (n=52). The primary endpoint was avoidance of respiratory failure within 72 h after extubation. Analysis was by intention to treat. This trial is registered with clinicaltrials.gov, identifier NCT00539708.

Findings Respiratory failure after extubation was less frequent in patients assigned non-invasive ventilation than in those allocated conventional oxygen therapy (8 [15%] vs 25 [48%]; odds ratio 5.32 [95% CI 2.11–13.46]; p<0.0001). In patients with respiratory failure, non-invasive ventilation as rescue therapy avoided reintubation in 17 of 27 patients. Non-invasive ventilation was independently associated with a lower risk of respiratory failure after extubation (adjusted odds ratio 0.17 [95% CI 0.06–0.44]; p<0.0001). 90-day mortality was lower in patients assigned non-invasive ventilation than in those allocated conventional oxygen (p=0.0146).

Interpretation Early non-invasive ventilation after extubation diminished risk of respiratory failure and lowered 90-day mortality in patients with hypercapnia during a spontaneous breathing trial. Routine implementation of this strategy for management of mechanically ventilated patients with chronic respiratory disorders is advisable.

Introduction

Reintubation is sometimes necessary for management of respiratory failure after extubation1 and is undertaken in 6–23% of patients within 48–72 h of planned extubation.2–4 Although reintubation could indicate increased disease severity, it is an independent risk factor for nosocomial pneumonia,5 mortality, and extended hospital stay.6 Findings of a case-control study4 suggest that non-invasive ventilation could be a promising treatment for respiratory failure after extubation, with potential to avoid reintubation.7 However, some concerns have been raised about use of non-invasive ventilation because in two randomised clinical trials in mixed populations, non-invasive ventilation was not beneficial in decreasing the risk of reintubation for patients who developed respiratory failure after extubation.8,9 By contrast, non-invasive ventilation implemented immediately after planned extubation was effective at avoiding respiratory failure in people at high risk of this complication who had tolerated a spontaneous breathing trial.8,9 Subgroup analysis showed that the benefits of non-invasive ventilation at enhancing survival were restricted to patients with hypercapnia (partial pressure of arterial carbon dioxide [PaCO₂] >45 mm Hg) during the spontaneous breathing trial before extubation.10 In this subset of patients, 98% had underlying chronic respiratory disorders.

Findings of an adequately powered clinical trial should be able to show benefits of non-invasive ventilation after extubation in a hypercapnic population for several reasons. First, definitive conclusions can be drawn, unlike with subgroup analyses. Second, the numbers of patients with hypercapnia enrolled into the study can be controlled, by comparison with low numbers recorded in previous subgroup analyses.10 Finally, non-invasive ventilation is an effective treatment for patients with acute-on-chronic hypercapnic respiratory failure.11 We postulated that early use of non-invasive ventilation during the initial period after extubation would avert respiratory failure and enhance survival of patients with chronic respiratory disorders who had hypercapnia during a spontaneous breathing trial before extubation. Therefore, we aimed to assess the effectiveness of this strategy compared with conventional oxygen management in patients who underwent planned extubation.

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Methods
Patients
We undertook a randomised controlled trial in the respiratory and medical intensive-care units of Hospital Clinic, Barcelona, and in the general intensive-care unit of Hospital Morales Meseguer, Murcia, Spain. All patients with chronic respiratory disorders, intubated for 48 h or more, who tolerated a spontaneous breathing trial through a T-piece after recovery of their disease, with hypercapnic respiratory failure (PaCO$_2$ >45 mm Hg) on spontaneous breathing, were deemed eligible for the study. We did not screen patients with a tracheostomy. Exclusion criteria were: facial or cranial trauma or surgery; recent gastric, oral, or oesophageal surgery (ie, during the current hospital admission); active upper gastrointestinal bleeding; excessive amount of respiratory secretions or weak cough; uncooperative state with inability to understand or unwillingness to follow the protocol’s instructions; upper-airway disorders; and previous decision to restrict therapeutic effort in the intensive-care unit. The ethics committee of each institution approved the study and we obtained written informed consent from all participants.

Procedures
We undertook a patient’s spontaneous breathing trial if the following criteria were met: improvement or resolution of the underlying cause of acute respiratory failure; correction of arterial hypoxaemia (partial pressure of arterial oxygen [PaO$_2$] >60 mm Hg at a fraction of inspired O$_2$ [FiO$_2$] ≤0.4 and positive end-expiratory pressure ≤5 cm H$_2$O); absence of fever (≥38°C) or hypothermia (<35°C); blood haemoglobin concentration of 70 g/L or more; haemodynamic stability; and alertness and ability to communicate. We obtained data for arterial blood gases before and at the end of the T-piece trial.

We defined failure of the spontaneous breathing trial as presence and persistence of one of the following criteria: respiratory frequency greater than 35 breaths per min; arterial O$_2$ saturation by pulse-oximetry less than 90% at FiO$_2$ of 0.4 or more; heart rate more than 140 beats per min or less than 50 beats per min; systolic blood pressure greater than 200 mm Hg or less than 70 mm Hg; diminished consciousness, agitation, or diaphoresis; and clinical signs suggestive of respiratory muscle fatigue, increased work of breathing, or both, such as use of respiratory accessory muscles, paradoxical motion of the abdomen, or retraction of the intercostal spaces. If no signs of failure appeared after 30–120 min, and arterial blood gases at the end of the spontaneous breathing trial showed PaCO$_2$ greater than 45 mm Hg, we proceeded with random allocation.

For research group details see http://www.idibapsrespiratoryresearch.org

Figure 1: Trial profile
*Previous decision to limit therapeutic effort in intensive-care unit (n=16); excessive amount of respiratory secretions (5); legal incapacity to give informed consent (3); upper-airway obstruction (2); incapacity for adequate follow-up due to transfer to another hospital (2); recent gastric (2) and oral (2) surgery, and active gastrointestinal bleeding (2).
We randomly allocated patients either non-invasive ventilation or conventional management (control); both procedures are described below. Three randomisation schedules were generated by computer for every intensive-care unit in random blocks of nine. Concealment was done with sequentially numbered opaque sealed envelopes, opened by the investigator only after informed consent was obtained. Patients and staff were aware of treatment allocations owing to the nature of the interventions.

Respiratory therapists implemented non-invasive ventilation (BiPAP Vision, Respironics, Murrysville, PA, USA), which included choice and fitting of masks, adjustment of ventilator settings, and initial adaptation of patients. Non-invasive ventilation was delivered continuously immediately after extubation using the bi-level positive-airway pressure mode. Therapists

adjusted inspiratory positive-airway pressure according to patients’ tolerance (12–20 cm H₂O) to achieve a respiratory rate less than 25 breaths per min. Expiratory positive-airway pressure was fixed at 5–6 cm H₂O and FiO₂ was set to achieve arterial O₂ saturation by pulse-oximetry of more than 92%. A face mask was used as first choice, and hydrocolloid dressing was applied systematically to prevent nasal-bridge damage. The procedure was delivered for as much time as possible for a scheduled maximum period of 24 h after extubation. After this time, non-invasive ventilation was withdrawn and patients received conventional venturi oxygen treatment for as long as they needed.

Patients allocated to the control group received conventional venturi oxygen treatment after extubation. Respiratory therapists delivered this intervention using conventional masks, without any dressing. We set FiO₂ to achieve arterial O₂ saturation of more than 92%. Conventional venturi oxygen was administered for as long as patients needed.

We continuously monitored patients’ electrocardiogram, pulse-oximetry, blood pressure, and respiratory rate. We measured arterial blood gases every 1–2 h after extubation or according to patients’ needs. We did not allow meals during the first 24 h after extubation to avoid aspiration. Cough and expectoration were assisted by respiratory therapists. We reviewed all relevant data from patients’ medical records and bedside flowcharts at entry and at the end of the study (72 h after extubation). We extended follow-up to 90 days after randomisation.

We informed all attending doctors of the characteristics of the study and explained predefined criteria for all relevant interventions and clinical decisions. Apart from the specific interventions of this trial, clinical management of patients during their stay in the intensive-care unit was undertaken according to the clinical protocols of the institutions.

We defined respiratory failure as presence and persistence for at least 30 min, within 72 h after extubation, of at least two of the following: respiratory acidosis (arterial pH <7·35 together with PaCO₂ >45 mm Hg); arterial O₂ saturation by pulse-oximetry of less than 90% or PaO₂, lower than 60 mm Hg at FiO₂ of 0·5 or more; respiratory frequency greater than 35 breaths per min; diminished consciousness, agitation or diaphoresis; and clinical signs suggestive of respiratory muscle fatigue, increased work of breathing, or both, such as use of respiratory accessory muscles, paradoxical motion of the abdomen, or retraction of intercostal spaces.19 We assigned causes to respiratory failure after extubation, with adapted published definitions:19 upper-airway obstruction; aspiration or excess respiratory secretions; congestive heart failure; respiratory failure; and encephalopathy.

We undertook immediate reintubation if any of the following predefined major clinical events arose: respiratory or cardiac arrest; respiratory pauses with
loss of consciousness or gasping for air; psychomotor agitation inadequately controlled by sedation; massive aspiration; persistent inability to remove respiratory secretions; heart rate below 50 beats per min with loss of alertness; and severe haemodynamic instability without response to fluids and vasoactive drugs.\textsuperscript{10,12} If a patient from either treatment group met criteria for respiratory failure after extubation, but did not fulfil criteria for immediate reintubation, we administered rescue therapy with non-invasive ventilation. For patients allocated non-invasive ventilation, rescue therapy consisted of re-institution or continuation of the procedure after 24 h of extubation. In addition to criteria for immediate reintubation, when patients who received rescue therapy with non-invasive ventilation showed deterioration of blood gases (arterial pH, PaCO\textsubscript{2}, PaO\textsubscript{2}) or tachyypnoea despite use of this method in optimum conditions, the procedure was not prolonged for more than 4 h\textsuperscript{14} and then patients were reintubated.

We defined clinical diagnoses of hospital-acquired pneumonia,\textsuperscript{15,16} purulent tracheobronchitis,\textsuperscript{9} and multiple organ failure\textsuperscript{8} according to published criteria. We recorded other relevant complications.

**Study endpoints**

The primary endpoint was rate of respiratory failure after extubation. The secondary endpoint was survival at 90 days (for the purposes of this report, we have used 90-day mortality).

**Statistical analysis**

Based on previous data in patients with hypercapnia,\textsuperscript{2} we expected a 41% rate of respiratory failure after extubation in patients assigned control and a prevalence of 15% in those assigned non-invasive ventilation. Initial calculations indicated a minimum sample size of 106 people (confidence level (1–α) 95%, power level (1–β) 80%).

We compared qualitative or categorical variables with χ\textsuperscript{2} or Fisher’s exact tests, when appropriate. We used the unpaired Student’s t test to compare quantitative continuous variables. We ascertained cumulative 90-day mortality probability with Kaplan-Meier curves and used the log-rank test to compare groups. We did analyses by intention to treat, and we set the level of significance at 0.05. We undertook univariate analyses of predictors of respiratory failure after extubation with the χ\textsuperscript{2} test and Student’s t test. We did multivariate analyses by logistic regression with a conditional stepwise forward model (p<0.05).

**Role of the funding source**

The sponsors of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had access to all the data of the trial and took full responsibility for the decision to submit for publication.

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### Results

Between May, 2005, and December, 2007, 164 consecutive patients were registered for the study, of whom 106 underwent random allocation (figure 1). 54 were allocated non-invasive ventilation and 52 were assigned control. General clinical characteristics and physiological variables of patients at entry into the study did not differ at baseline (tables 1 and 2).

Non-invasive ventilation was delivered for a mean period of 18 h (SD 7) in patients assigned to this group. Mean levels of inspiratory and expiratory positive-airway pressure in these patients were 17 cm H\textsubscript{2}O (SD 3) and 6 cm H\textsubscript{2}O (1), respectively. Five (10%) people assigned non-invasive ventilation tolerated the procedure for 6 h or less.

Table 3 summarises outcome variables in the trial. Respiratory failure after extubation arose in fewer patients allocated non-invasive ventilation than those assigned control. The main difference between groups in respiratory failure was noted within 24 h after extubation (figure 2), whereas in the following 2 days, incidence was similar between groups.

In patients who developed respiratory failure after extubation but who did not need immediate reintubation, non-invasive ventilation as rescue therapy resulted in avoidance of reintubation in two of seven patients assigned non-invasive ventilation and 15 of 20 controls. One patient from the control group refused reintubation. Hence, the reintubation rate did not differ by much in the non-invasive ventilation group.

Of variables associated with respiratory failure after extubation in univariate analyses, use of non-invasive ventilation was associated independently with decreased risk for this complication (table 4). The variables tested for association with respiratory failure after extubation were those available before extubation: age, sex, comorbidities, causes of mechanical ventilation, severity scores, modes of ventilation and previous duration of ventilation, forced spirometry values, and physiological variables before and at the end of the spontaneous breathing trial.

### Table 2: Physiological variables of patients at entry into the study

<table>
<thead>
<tr>
<th>Variable</th>
<th>Non-invasive ventilation (n=54)</th>
<th>Control (n=52)</th>
<th>Non-invasive ventilation (n=54)</th>
<th>Control (n=52)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Respiratory frequency</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(breaths per min)</td>
<td>18 (4)</td>
<td>17 (3)</td>
<td>23 (5)</td>
<td>23 (5)</td>
</tr>
<tr>
<td>f/V</td>
<td>–</td>
<td>–</td>
<td>64 (26)</td>
<td>65 (23)</td>
</tr>
<tr>
<td>Heart rate (beats per min)</td>
<td>82 (15)</td>
<td>77 (16)</td>
<td>89 (13)</td>
<td>87 (16)</td>
</tr>
<tr>
<td>Systolic blood pressure</td>
<td>132 (17)</td>
<td>128 (21)</td>
<td>146 (18)</td>
<td>141 (26)</td>
</tr>
<tr>
<td>(mm Hg)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Arterial pH</td>
<td>7.41 (0.05)</td>
<td>7.41 (0.05)</td>
<td>7.38 (0.04)</td>
<td>7.38 (0.03)</td>
</tr>
<tr>
<td>PaCO\textsubscript{2} (mm Hg)</td>
<td>48 (6)</td>
<td>48 (7)</td>
<td>55 (6)</td>
<td>53 (5)</td>
</tr>
<tr>
<td>PaO\textsubscript{2} (mm Hg)</td>
<td>88 (20)</td>
<td>93 (17)</td>
<td>76 (14)</td>
<td>81 (17)</td>
</tr>
<tr>
<td>PaO\textsubscript{2}/FiO\textsubscript{2}</td>
<td>227 (51)</td>
<td>246 (49)</td>
<td>198 (39)</td>
<td>206 (40)</td>
</tr>
</tbody>
</table>

Data are mean (SD). f/V= respiratory frequency to tidal volume ratio. *Variables obtained at end of breathing trial.
Main causes of respiratory failure after extubation

- Respiratory failure
- Aspiration or excess respiratory secretions
- Cardiac failure
- Upper-airway obstruction
- Encephalopathy

Time from extubation to respiratory failure (h)

- Control (n=52)
- Non-invasive ventilation (n=54)

<table>
<thead>
<tr>
<th>Outcome variables</th>
<th>Non-invasive ventilation (n=54)</th>
<th>Control (n=52)</th>
<th>Odds ratio (95% CI)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Respiratory failure after extubation</td>
<td>8 (15%)</td>
<td>25 (48%)</td>
<td>5.32 (2.31-13.46)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Main causes of respiratory failure after extubation</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Respiratory failure</td>
<td>3</td>
<td>18</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aspiration or excess respiratory secretions</td>
<td>3</td>
<td>3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardiac failure</td>
<td>1</td>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Upper-airway obstruction</td>
<td>0</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Encephalopathy</td>
<td>1</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Time from extubation to respiratory failure (h)</td>
<td>29 (13)</td>
<td>17 (18)</td>
<td></td>
<td>0.0982</td>
</tr>
<tr>
<td>Criteria met for reintubation</td>
<td>6 (11%)</td>
<td>10 (19%)</td>
<td>1.90 (0.64-5.68)</td>
<td>0.3741</td>
</tr>
</tbody>
</table>

Complications

- Tracheostomy needed | 3 (6%) | 2 (4%) | 0.68 (0.11-4.24) | 0.8675 |
- Infections diagnosed after study onset | | | | |
- Ventilator-associated pneumonia | 3 (6%) | 9 (17%) | 3.48 (0.89-13.70) | 0.1230 |
- Ventilator-associated tracheobronchitis | 1 (2%) | 1 (2%) | | |
- Catheter-related infection | 1 (2%) | 2 (4%) | | |
- Urinary-tract infection | 2 (4%) | 0 | | |
- Bacteraemia of unknown origin | 1 (2%) | 0 | | |

Length of stay

- Intensive-care unit stay (days) | 11 (13) | 10 (9) | | 0.5041 |
- Hospital stay (days) | 29 (27) | 24 (17) | | 0.2988 |

Mortality

- Intensive-care unit mortality | 3 (6%) | 4 (8%) | 1.42 (0.30-6.67) | 0.7132 |
- Hospital mortality | 6 (11%) | 11 (22%) | 2.25 (0.73-6.33) | 0.2587 |
- Mortality at 90 days | 6 (11%) | 16 (31%) | 3.56 (1.27-10.0) | 0.0244 |
- Causes of death within 90 days after entry into the study | | | | |
- Respiratory failure | 0 | 7 | | 0.2037 |
- Shock or multiple organ failure | 3 | 3 | | |
- Cardiac arrest | 2 | 3 | | |
- Other | 1 | 3 | | |

Table 3: Outcome variables, length of stay, and causes of death

Discussion

The results of our study confirm the benefits of early use of non-invasive ventilation after extubation to diminish risk of respiratory failure in patients with chronic respiratory disorders and hypercapnia during a spontaneous breathing trial. This strategy resulted in lowered mortality in our population.

This specific population is at high risk of development of respiratory failure after extubation, confirmed by a frequency of 48% in the control group, similar to a 41% rate recorded in a previous trial. By contrast, prevalence of respiratory failure after planned extubation was substantially lower—25% and 23%—in previous trials undertaken in mixed populations of patients with a low proportion of chronic respiratory disorders and hypercapnia. Therefore, development of hypercapnia after an otherwise satisfactory breathing trial could be an indication that the patient is not ready for extubation and is a marker for continued support by ventilation.

About two-thirds of all patients who developed respiratory failure after extubation but who did not need immediate reintubation benefited from rescue therapy with non-invasive ventilation; this success rate was 75% in patients assigned control, who had not received non-invasive ventilation previously. The real effectiveness and relevance of rescue therapy with non-invasive ventilation is, however, uncertain because it was not applied randomly. Further demonstration of superiority over standard medical treatment would need a randomised clinical trial. Of 17 patients who did not need reintubation after rescue therapy, only one died in hospital. The good outcome of successful rescue therapy with non-invasive ventilation accords with previous results.

By contrast with our findings, in mixed populations of patients with respiratory failure after extubation, use of non-invasive ventilation to avoid reintubation was successful in fewer patients (52% and 28%), with no advantages noted over standard medical treatment. Non-invasive ventilation even resulted in higher mortality in those who needed reintubation and who received non-invasive ventilation, compared with patients who received standard medical treatment, and these researchers therefore discouraged use of non-invasive ventilation for this indication. Raised mortality was attributed to an extended time from extubation to reintubation, which is an independent risk factor for increased mortality in reintubated patients, in individuals who received non-invasive ventilation.

However, in our study, the hospital mortality rate of patients who were reintubated directly was similar to that of people who were reintubated after failure of rescue therapy with non-invasive ventilation (67% and 70%, respectively). In addition, rescue therapy with non-invasive ventilation did not result in delayed reintubation compared with patients directly reintubated, since the median time from extubation to reintubation was 26 h.
(IQR 9–36) in patients who received rescue therapy compared with 35 h (2–44) in those who were reintubated directly. This finding indicates that rescue therapy with non-invasive ventilation is safe and can provide a useful alternative to reintubation in patients with hypercapnia and chronic respiratory disorders who do not meet major criteria for reintubation.

Hypercapnia during a spontaneous breathing trial is associated with poor survival in mechanically ventilated patients, particularly when no ventilation support is provided after extubation. Our data confirm these findings. Therefore, this population is the target for early institution of non-invasive ventilation for prevention of further respiratory distress. Similarly, individuals with severe hypercapnic respiratory failure secondary to exacerbations of chronic obstructive pulmonary disease are among the best responders to non-invasive ventilation, even when they present other concomitant acute diseases such as community-acquired pneumonia or cardiogenic pulmonary oedema.

In our study, the 90-day mortality rate was reduced with non-invasive ventilation. The few patients from the non-invasive ventilation group who needed reintubation—a major determinant of poor survival—could account partly for this finding. However, more individuals assigned control did not need reintubation after rescue therapy with non-invasive ventilation than those allocated non-invasive ventilation (15 vs 2). Therefore, the reintubation rate of each group was similar compared with the large difference in rate of respiratory failure after extubation between groups, suggesting a protective effect of non-invasive ventilation beyond reduction of reintubation. In the same way, differences in mortality between both groups arose later after discharge from the intensive-care unit. Similar long-term benefits of non-invasive ventilation have been described. The potential mechanism of this protective effect of non-invasive ventilation deserves further investigation.

Other reasons that could account for the effectiveness of non-invasive ventilation is our use of a ventilator specifically designed for this procedure, which includes control of FiO2, effective compensation for leaks, real-time assessment of mask pressure, and a sensitive and rapid response flow-by trigger, as done in previous trials. This ventilator is widely used with similar settings to those in the present study. The feasibility to undertake this protocol in clinical practice helps generalise our results. By contrast, researchers on previous negative studies either used a ventilator with reduced performance or did not choose a specific ventilator for the trial. Finally, non-invasive ventilation was applied continuously after extubation, as done previously. This methodological point is key in our study, since intermittent use of non-invasive ventilation for prolonged periods resulted in limited clinical effectiveness.

Several limitations of our study should be taken into account. First is the difficulty for correct masking of investigators, attending doctors, and patients, a common bias in this type of open clinical trial. Despite the fact that we predefined criteria for all relevant interventions, clinical decisions, and outcome variables, this bias could not be controlled entirely. Masking the control group with low levels of continuous positive airway pressure would probably result in substantial bias since this technique is expected to decrease the work of breathing in these patients. Second, rescue therapy with non-invasive ventilation might have affected survival between groups, since many patients assigned control did not need reintubation. Third, our trial was undertaken at two centres with lengthy experience of use of non-invasive ventilation. This factor could have affected success of this technique. However, good tolerance of non-invasive ventilation by
conscious patients with hypercapnia facilitates use of this technique in centres with reduced experience.

In conclusion, early use of non-invasive ventilation after extubation diminished risk of respiratory failure after extubation and reduced 90-day mortality in patients with hypercapnia after a spontaneous breathing trial. This trial confirms the effectiveness of non-invasive ventilation in this clinical setting and provides scientific evidence for routine implementation of this strategy for management of mechanically ventilated patients with chronic respiratory disorders.

Contributors
MF had the idea for the study and helped with its design, contributed to data collection, analysed and interpreted data, and wrote the report. AT had the idea for the study and supervised the study, and helped to write the report. JS, MV, AC, GG, JRB, and JMN contributed to data collection.

Conflicts of interest
We declare that we have no conflicts of interest.

Acknowledgments
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