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Leaving invasive ventilation behind

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See [Articles](#) page 1082

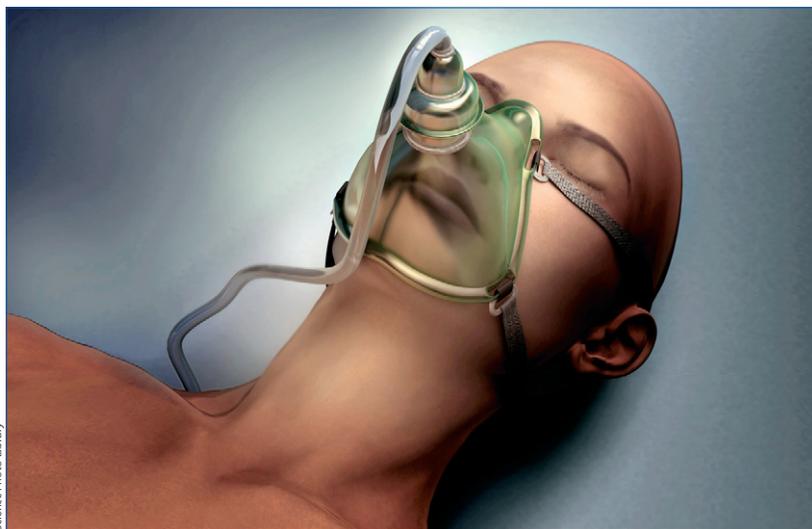
The ability to assist ventilation, usually by addition of inspiratory pressure support with increased expiratory pressure, is the essence of non-invasive ventilation. This technique reduces the work of breathing, decreases ventilatory drive and respiratory rate, boosts tidal volume and alveolar ventilation, and can be applied with a nasal or full facemask without compromising the defences of the upper airway.¹ When given to patients with decompensated hypercapnic respiratory failure, typically due to chronic obstructive pulmonary disease, non-invasive ventilation is effective. The method can be used outside the intensive-care unit² and has a substantial evidence base.³ Unsurprisingly, non-invasive ventilation has been used to treat other forms of respiratory failure—including patients with cardiogenic pulmonary oedema—and as an aid to weaning patients from invasive mechanical ventilation.

However, findings of an adequately powered randomised controlled trial showed that, contrary to data of previous systematic reviews,^{4,5} non-invasive ventilation

and continuous positive airway pressure were no better than was standard treatment for management of cardiogenic pulmonary oedema.⁶ Similar issues arose when non-invasive ventilation was tested as an aid to weaning of patients from mechanical ventilation in the general intensive-care unit. Results of early small trials were challenged when those of comparatively larger studies noted no benefit of this technique during weaning.^{7,8} However, in a subanalysis by Ferrer and colleagues of 162 Spanish patients,⁹ those who developed hypercapnic respiratory failure secondary to chronic respiratory disease seemed to benefit from non-invasive ventilation.

In *The Lancet* today, Miquel Ferrer and colleagues¹⁰ have tested their previous hypothesis in 106 patients with chronic lung disease who developed hypercapnia during a spontaneous breathing (weaning) trial. Since development of hypercapnia was not a criterion for weaning failure, these researchers randomly allocated patients to either support with non-invasive ventilation (average of 18 h in total) or conventional oxygen treatment. They reported that the group allocated non-invasive ventilation had a lower rate of reintubation and reduced 90-day mortality. Patients who failed with the conventional weaning protocol were offered non-invasive ventilation and many of these individuals could be managed without reintubation, suggesting that non-invasive ventilation was beneficial.

So why did these results differ from those in the previous trials? In studies from the general intensive-care unit, only a few patients enrolled had chronic respiratory disease, with sepsis, trauma, and pneumonia being much more frequent reasons for institution of ventilation.^{7,8} This finding is supported by comparison of APACHE-II (acute physiology and chronic health evaluation-II) scores, which were similar at initiation of weaning in these



previous studies to those on admission in today's report. This explanation also accounts for the shorter period of preweaning ventilation in the current study compared with previous trials (4–5 days vs 6–8 days).

Some issues remain unclear. 13% of patients in today's study had received non-invasive ventilation previously. Might more people have avoided invasive ventilation altogether had non-invasive ventilation been offered as their primary treatment? Similarly, how many patients reintubated despite non-invasive ventilation had a complex illness at their initial clinical presentation?

Three further points are worth making. First, all papers discussed here are of a high standard scientifically and methodologically, and show how high-quality clinical research in the intensive-care unit can affect everyday practice.¹¹ Second, prospective testing of the conclusion of a post-hoc analysis is the only way to avoid the pitfalls of such an analytical approach.¹² Defining a subgroup of patients—in this case, those with hypercapnia on weaning with a history of chronic respiratory disease—who were helped substantially by non-invasive ventilation moves clinical care forward. Third, although considerable therapeutic nihilism has been reported about use of invasive ventilation for management of individuals with chronic obstructive pulmonary disease in the UK,¹³ these new data show that such patients spend less time in the intensive-care unit than do others receiving invasive ventilation, and when non-invasive ventilation is used they wean successfully. Hopefully, data such as these will change our perceptions of how and when aggressive treatment should be offered to the many patients with chronic obstructive pulmonary disease who still need this form of help.

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I declare that I have no conflicts of interest.

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Benchmarking in surgical research

Surgical care is an integral part of health care throughout the world. An estimated 234 million operations take place each year, a volume that now exceeds that of childbirth.¹ Surgery can effectively treat the important chronic diseases of the 21st century, including cancer, obesity, and cardiovascular disease.^{2,3} Academic surgery drives innovation and improvement in surgical outcomes, although it continues to be underfunded and poorly supported.⁴

An influential editorial in *The Lancet* in 1996 justifiably questioned the future of surgical research, associating it with the term comic opera.⁵ The paucity of randomised trials coupled with a lack of basic scientific research had led to an inability to achieve the highest levels of evidence.⁶ This situation triggered a constructive debate in the research community to identify areas in which academic surgery requires improvement.

See [Editorial](#) page 1037

See [Perspectives](#) page 1057

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

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Summary

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See [Comment](#) page 1044

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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.

Funding IDIBAPS, CibeRes, Fondo de Investigaciones Sanitarias, European Respiratory Society.

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.²

Findings of a case-control study⁶ 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.¹⁸ 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.^{9,10} 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 [PaCO_2] >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.

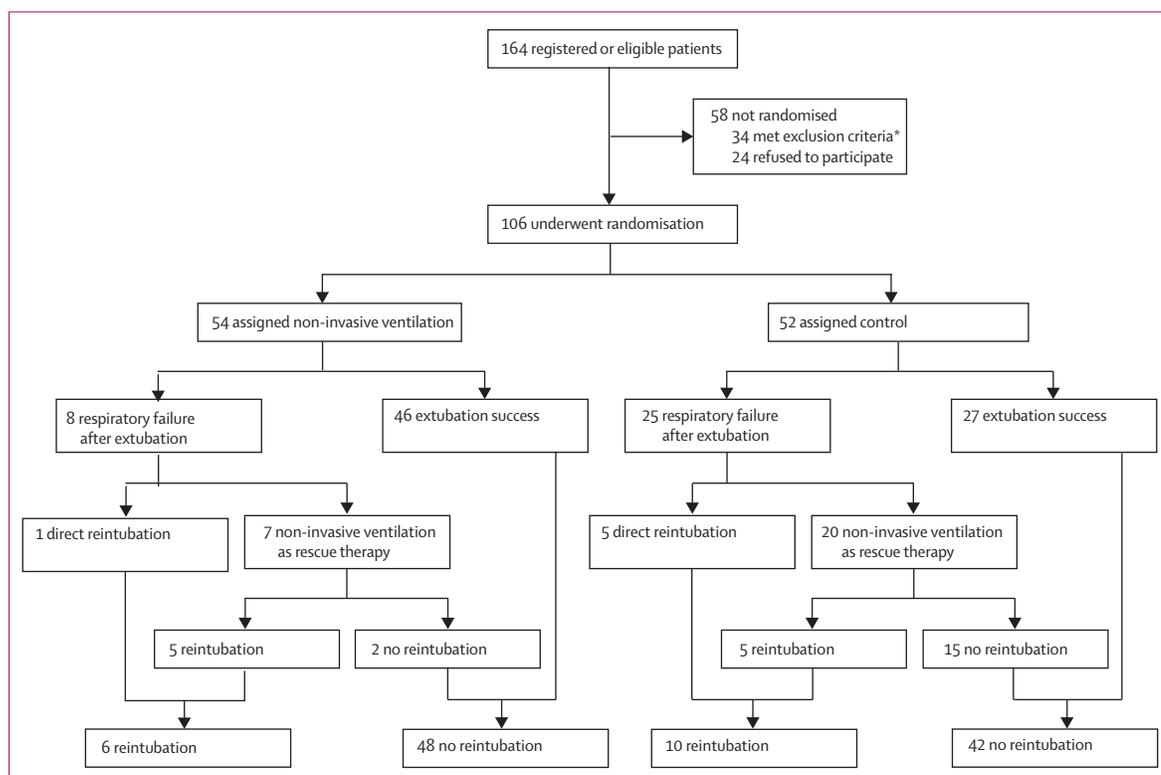


Figure 1: Trial profile

*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).

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 ($\text{PaCO}_2 > 45$ 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_2O); absence of fever ($\geq 38^\circ\text{C}$) or hypothermia ($< 35^\circ\text{C}$); blood haemoglobin concentration of 70 g/L or more; haemodynamic stability; and alertness and ability to communicate.^{10,12} 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.^{10,12} 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>

	Non-invasive ventilation (n=54)	Control (n=52)
Age (years)	67 (10)	70 (9)
Men	44 (81%)	36 (69%)
APACHE-II score on admission	20 (7)	20 (7)
APACHE-II score at entry into the study	11 (3)	11 (3)
Previous duration of mechanical ventilation (days)	5 (3)	4 (2)
Forced expiratory volume in 1 s (% predicted)	34 (13)	38 (11)
Type of chronic respiratory disease		
COPD or chronic bronchitis*	38 (70%)	36 (69%)
Sequelae of pulmonary tuberculosis	7 (13%)	6 (12%)
Bronchiectasis	2 (4%)	4 (8%)
Obesity-hypoventilation syndrome	5 (9%)	4 (8%)
Chest-wall deformity	1 (2%)	1 (2%)
Chronic persistent asthma	1 (2%)	1 (2%)
Other comorbidities		
Chronic heart disorders†	19 (35%)	27 (52%)
Immunosuppression‡	2 (4%)	2 (4%)
Diabetes mellitus	11 (20%)	13 (25%)
Liver cirrhosis	3 (6%)	1 (2%)
Neoplasm	2 (4%)	4 (8%)
Chronic renal failure	1 (2%)	1 (2%)
Previous use of non-invasive ventilation in hospital	7 (13%)	7 (13%)
Causes of mechanical ventilation		
Exacerbation of chronic respiratory disorder	28 (52%)	25 (48%)
Pneumonia	7 (13%)	7 (13%)
Congestive heart failure	5 (9%)	8 (15%)
Neurological disease	1 (2%)	2 (4%)
Sepsis	6 (11%)	5 (10%)
Postoperative respiratory failure	3 (6%)	2 (4%)
Other	4 (7%)	3 (6%)

Data are mean (SD) or number of patients (%). APACHE-II=acute physiology and chronic health evaluation-II. COPD=chronic obstructive pulmonary disease. Pulmonary function tests were available in 66 (62%) patients.
 *Chronic bronchitis defined by history of dyspnoea, cough, expectoration, and smoke consumption without pulmonary function testing. †Includes coronary-artery disease, hypertensive or valvular heart diseases, and dilated myocardial disease of any cause. ‡Includes neutropenia after chemotherapy or bone-marrow transplant, drug-induced immunosuppression in solid-organ transplant or as a result of corticosteroids or cytotoxic therapy, and HIV-related disorders.

Table 1: Baseline characteristics of patients at entry into the study

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.¹⁰ We assigned causes to respiratory failure after extubation, with adapted published definitions:¹³ 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.^{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 reinstatement 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, PaCO₂, PaO₂) or tachypnoea despite use of this method in optimum conditions, the procedure was not prolonged for more than 4 h¹⁴ and then patients were reintubated.

We defined clinical diagnoses of hospital-acquired pneumonia,^{15,16} purulent tracheobronchitis,¹⁷ and multiple organ failure¹⁸ 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,¹⁰ 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^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^2 test and Student's *t* test. We did multivariate analyses by logistic regression with a conditional stepwise forward model ($p_{in} < 0.10$).

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.

	Mechanical ventilation		Spontaneous breathing trial*	
	Non-invasive ventilation (n=54)	Control (n=52)	Non-invasive ventilation (n=54)	Control (n=52)
Respiratory frequency (breaths per min)	18 (4)	17 (3)	23 (5)	23 (5)
f/V _T	64 (26)	65 (23)
Heart rate (beats per min)	82 (15)	77 (16)	89 (13)	87 (16)
Systolic blood pressure (mm Hg)	132 (17)	128 (21)	146 (18)	141 (26)
Arterial pH	7.41 (0.05)	7.41 (0.05)	7.38 (0.04)	7.38 (0.03)
PaCO ₂ (mm Hg)	48 (6)	48 (7)	55 (6)	53 (5)
PaO ₂ (mm Hg)	88 (20)	93 (17)	76 (14)	81 (17)
PaO ₂ /FiO ₂	227 (51)	246 (49)	198 (39)	206 (40)

Data are mean (SD). f/V_T=respiratory frequency to tidal volume ratio. *Variables obtained at end of breathing trial.

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

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 H₂O (SD 3) and 6 cm H₂O (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.

	Non-invasive ventilation (n=54)	Control (n=52)	Odds ratio (95% CI)	p
Outcome variables				
Respiratory failure after extubation	8 (15%)	25 (48%)	5.32 (2.11–13.46)	<0.0001
Main causes of respiratory failure after extubation			..	0.3451
Respiratory failure	3	18		
Aspiration or excess respiratory secretions	3	3		
Cardiac failure	1	2		
Upper-airway obstruction	0	1		
Encephalopathy	1	1		
Time from extubation to respiratory failure (h)	29 (13)	17 (18)	..	0.0982
Criteria met for reintubation	6 (11%)	10 (19%)	1.90 (0.64–5.68)	0.3741
Complications				
Tracheostomy needed	3 (6%)	2 (4%)	0.68 (0.11–4.24)	0.9675
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%)	2.15 (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			..	0.2037
Respiratory failure‡	0	7		
Shock or multiple organ failure	3	3		
Cardiac arrest	2	3		
Other	1	3		

Data are mean (SD) or number of patients (%). *Catheter-related sepsis defined as positive blood and catheter cultures concomitant with inflammatory signs in a catheterised vein or at its insertion point. †Urinary-tract infection defined as presence of amplified leucocytes in urinary sediment examination together with a positive semiquantitative urine culture. ‡Death after progressive hypoxaemia, hypercapnia, or both, without other major organ system failures.

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

Lengths of stay in the intensive-care unit and in hospital were similar in patients from each group. Specific complications associated with non-invasive ventilation included nasal-bridge damage in five patients (10%), conjunctivitis in two (4%), and gastric distension in two (4%).

Mortality in the intensive-care unit and the hospital did not differ significantly between groups. However, 90-day mortality ($p=0.0146$; figure 3) was significantly lower in patients assigned non-invasive ventilation than in those allocated control. Table 3 shows causes of death within 90 days of randomisation.

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.¹⁰ 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.¹⁸ 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.¹⁰

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%¹ and 28%⁸), 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,¹ 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,¹³ in individuals who received non-invasive ventilation.¹

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

conscious patients with hypercapnia¹² 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 helped with its design, 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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