Noninvasive Positive-Pressure Ventilation for Postextubation Respiratory Distress

A Randomized Controlled Trial

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Context Noninvasive positive-pressure ventilation (NPPV) has been demonstrated to be effective in preventing the need for endotracheal intubation in some patients who present with acute respiratory failure. It is also used for patients who develop acute respiratory distress after extubation, but there are no randomized controlled trials that address its effectiveness in this population.

Objective To determine the effectiveness of NPPV compared with standard medical therapy in preventing the need for endotracheal reintubation in high-risk patients who develop respiratory distress during the first 48 hours after extubation.

Design Randomized, controlled, unblinded study with concealed allocation conducted between August 1, 1996 and October 31, 1999.

Setting An intensive care unit (ICU) in an academic, tertiary care hospital in Ontario.

Patients Eighty-one patients with a history of cardiac or respiratory disease or who initially required ventilatory support for more than 2 days and who developed respiratory distress within 48 hours of extubation.

Interventions Patients were randomly assigned to receive standard medical therapy alone (supplemental oxygen to maintain oxygen saturation by pulse oximetry ≥95%; n=42) or NPPV by face mask plus standard medical therapy (n=39).

Main Outcome Measures Rates of reintubation, duration of mechanical ventilation, lengths of ICU and hospital stay, and hospital mortality.

Results Comparing the NPPV group with the standard-therapy group, there was no difference in the rate of reintubation (72% vs 69%; relative risk, 1.04; 95% confidence interval, 0.78-1.38) or hospital mortality (31% for both groups; relative risk, 0.99; 95% confidence interval, 0.52-1.91). Similarly, no difference was found in duration of mechanical ventilation or length of ICU or hospital stay.

Conclusions The addition of NPPV to standard medical therapy does not improve outcome in heterogeneous groups of patients who develop respiratory distress during the first 48 hours after extubation.

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THE USE OF NONINVASIVE POSITIVE-PRESSURE VENTILATION (NPPV) in acute respiratory failure to avoid the need for endotracheal intubation was first reported in the late 1980s by Meduri et al.[1] The apparent successful application of this form of ventilation in this and other case series[2-8] has led to more intensive scrutiny of this technology in randomized controlled trials.[9-27] It appears that successful avoidance of endotracheal intubation through the addition of NPPV may depend on the population studied.[28] Although most trials have demonstrated the potential benefit of NPPV for patients who present with acute exacerbations of chronic obstructive pulmonary disease (COPD),[9-19] less evidence has been published that has consistently supported its benefit for other patient groups.[20-24]

Noninvasive positive-pressure ventilation has also been used to decrease the duration of mechanical ventilation for patients who require endotracheal intubation. For these patients, NPPV has been applied in 1 of 3 ways: (1) as an adjunct to weaning patients from mechanical ventilation by early extubation directly to

See also Patient Page.

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NPPV,[25,26] (2) as a routine application of NPPV to all patients or a selected group of higher-risk patients who were extubated at the time they fulfilled standard extubation criteria,[27] or (3) as an application of NPPV only to patients who develop respiratory distress after having been extubated according to standard criteria.[29] Two randomized controlled trials suggested that although directly extubating patients to NPPV is potentially beneficial for patients with COPD (decreased length of stay and mortality),[25] the effect is less clear for a more heterogeneous population.[26] The only trial applying NPPV directly after patients are either electively or self-extubated found no benefit from the addition of NPPV.[27] To date, no randomized controlled trial has been reported on the potential benefit of NPPV for patients who develop respiratory distress after extubation. Our hypothesis was that the addition of NPPV to standard therapy for patients who develop respiratory distress after extubation would decrease the need for reintubation. The objective of this trial was to determine the relative effectiveness of NPPV compared with standard medical therapy in preventing the need for endotracheal reintubation in high-risk patients who develop respiratory distress during the first 48 hours after extubation.

METHODS

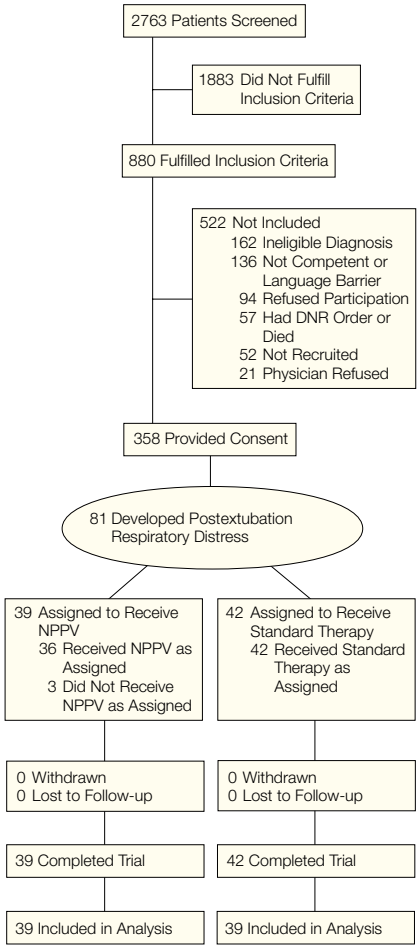
Patients

Between August 1, 1996, and October 31, 1999, patients who required ventilatory support for more than 48 hours or had a history of either congestive heart failure or chronic lung disease or their surrogate decision makers were approached for consent to participate in this study just before or shortly following their extubation. Patients were only included in the study if they developed respiratory distress, defined as a respiratory rate of greater than 30/min or an increase in respiratory rate of greater than 50% from baseline or use of accessory muscles of respiration or abdominal paradox.

The following specific extubation criteria guided the timing of extubation for all intensive care unit (ICU) patients irrespective of their potential eligibility for the study: reason for intubation had been reversed; patients were awake, afebrile, and able to protect their airway; and patients had a maximal negative inspiratory pressure greater than –20 cm H_2O, a vital capacity of greater than 10 mL/kg, a respiratory rate of less than 25/min, and a level of ventilatory support of less than 10 cm H_2O of pressure support. Patients were excluded if they had a do-not-resuscitate order; had a prior history of obstructive sleep apnea, cervical spine injury, or upper airway obstruction; were mentally challenged; or were judged incompetent with no available surrogate decision maker. Patients were also excluded if a language barrier existed, if they had been previously randomized in the study, or if they developed respiratory distress outside the ICU (because the goal was to identify respiratory distress early and react to it by initiating NPPV quickly in those randomized to receive this treatment). After the first year, patients with an acute exacerbation of COPD were excluded because the randomized trial evidence strongly supported the use of NPPV for these patients[9-11] and because NPPV was therefore applied when these patients developed respiratory distress. The study was conducted in the ICU at the London Health Sciences Centre, Victoria Campus, British Columbia, a 30-bed tertiary care ICU that serves as the only location in the hospital where patients receive mechanical ventilation. In addition to medical and surgical patients, this ICU also cares for post–cardiac surgery patients and multiple-trauma patients. The study protocol was approved by the review board for health sciences research involving human subjects at the University of Western Ontario, London, Ontario. Informed consent was obtained from all patients or their surrogate decision makers.

Following extubation, patients who gave consent to participate were followed up for the remainder of their hospital stay. If they developed respiratory distress within the first 48 hours of extubation and were still in the ICU, they were randomized to receive NPPV or standard therapy. Consent was obtained just before extubation or as soon as possible after extubation to avoid having to obtain consent from patients in acute respiratory distress. This resulted in a small portion of consenting patients who were eventually randomized (FIGURE).

Figure. Randomization of Patients



Diagnostic group refers to those patients excluded because of diagnostic group as outlined in the "Methods" section (chronic obstructive pulmonary disease after the first year, spinal cord injury, obstructive sleep apnea). It is not possible to provide numbers for those patients who met inclusion and exclusion criteria but were not approached for consent (patient or physician refusal or no apparent attempt made to recruit the patient) who developed respiratory distress (ie, would have been eligible for the study) because this was not recorded. Of those randomized, the flow of patients through the trial is also illustrated. DNR indicates do not resuscitate; NPPV, noninvasive positive-pressure ventilation.

The unit of randomization was the individual patient, and randomization was concealed using opaque envelopes. The randomization schedule was computer generated by an epidemiologist, who was otherwise not part of the study, using random blocks of 4, 6, or 8. The study coordinator prepared sealed opaque envelopes, and individual envelopes were drawn by the respiratory therapist caring for the patient at the time of randomization.

Standard Therapy

Patients assigned to standard therapy received supplemental oxygen to maintain oxygen saturation by pulse oximetry greater than or equal to 95%. In addition, they received aggressive physiotherapy and pharmacotherapy with diuretics, inhaled β-agonists, and inhaled ipratropium bromide as clinically indicated. The attending ICU staff made decisions regarding the use of these interventions.

NPPV Treatment

Patients randomized to NPPV received ventilatory support in addition to standard therapy (BiPAP S/T-D30 Ventilatory Support System, Respironics Inc, Murrysville, Pa). The ventilatory support device is capable of providing independently adjustable inspiratory positive airway pressures (IPAPs) and expiratory positive airway pressures (EPAPs). The device had been used for a year in the ICU before initiating the study. In addition, the respiratory therapist staff received extensive in-service training before the study and once again during the study and informal in-service training throughout the trial. The ventilatory support system was initiated using a specific protocol designed by the respiratory therapy department and critical care unit staff. The ventilatory support system was initiated at a level of 4 cm H_2O of EPAP and 9 cm H_2O of IPAP in a spontaneous mode. For hypoxemic respiratory failure, EPAP was titrated in increments of 2 cm H_2O while keeping IPAP at a fixed increment above EPAP to achieve an oxygen saturation of greater than 92%. For hypercapnic respiratory failure, IPAP was titrated in increments of 2 cm H_2O following tidal volumes and respiratory rate. The objectives were to have the patient breathing comfortably as evidenced by a decrease in respiratory rate and heart rate with oxygen saturations greater than 92% and a normal pH on arterial blood gases. Throughout the first hour, respiratory therapists continually reassessed patients, first explaining how NPPV works and providing continual reassurance to the patients. The goal was to apply NPPV continually for the first 12 hours, and then nonassisted breathing would be allowed intermittently at increasing intervals provided patients were breathing comfortably, their oxygenation remained adequate, and their arterial pH was greater than 7.35. Noninvasive positive-pressure ventilation was reinstated using the same criteria for respiratory distress. The attending physicians were given control over this weaning process. Full face mask was the preferred interface and was used exclusively after the first few patients. Noninvasive positive-pressure ventilation was applied only in the ICU in this study.

Criteria for Intubation

We developed the following guidelines for endotracheal intubation. Patients were to be strongly considered for intubation if they consented to intubation *and* any of the following criteria were met: cardiac arrest *or* respiratory arrest *or* apnea with loss of consciousness or gasping for air (inability to protect airway) *or* marked respiratory distress in extremis *or* psychomotor agitation making nursing care impossible and requiring sedation *or* heart rate of less than 50/min with loss of alertness *or* hemodynamic instability with systolic arterial pressure below 70 mm Hg.

Follow-up

At baseline, demographic data, Acute Physiology and Chronic Health Evaluation II (APACHE II) score, and diagnosis were recorded for all patients. Duration of mechanical ventilation before initial extubation was recorded, as were the following weaning parameters when available: vital capacity, minute ventilation, respiratory rate, and maximal negative inspiratory pressure. At the time of randomization, respiratory rate, heart rate, blood pressure, arterial blood gases, and fraction of inspired oxygen (FIO_2) were recorded. For those patients randomized to receive NPPV, the time to application of NPPV, the initial settings used for IPAP and EPAP, and whether the patient tolerated NPPV (able to wear as requested by respiratory therapist) were recorded. Patients were followed up throughout their ICU and hospital stays. The need for reintubation was recorded as were the duration of further conventional mechanical ventilation (not NPPV), the length of ICU and hospital stay, and vital status on discharge from ICU and hospital. We recorded whether a patient developed pneumonia, accepting the clinical diagnosis made by attending physicians rather than predefining specific criteria.

Sample Size and Statistical Analysis

After reviewing reintubation rates within our ICU and the literature, a baseline reintubation rate of 65% was estimated for this higher-risk group. Using a type I error of 5%, we estimated that we would need 40 patients in each group to have a power of 80% to detect a reduction in reintubation rate to 35%. The latter was a rate that was suggested as reasonable from the available literature. A total of 81 patients were randomized.

Baseline comparison of the 2 study groups was conducted using the χ^2 statistic or Fisher exact test, where appropriate, for categorical variables and the *t* test for continuous variables. The primary outcome of need for intubation was tested using the χ^2 statistic, as were the secondary outcomes of ICU and hospital survival. Secondary outcomes of duration of ventilation and ICU and hospital length of stays were compared using both the 2-sample *t* test and the Mann-Whitney *U* test for means and medians, respectively. Survival analysis was

used to compare the time to intubation for those patients who required intubation. All analyses were conducted on patients within their randomized groups (intention-to-treat analyses).

Because of concerns regarding the potential for selection bias (the systematic withholding of patients from the study that may benefit from NPPV, therefore biasing the study toward demonstrating no treatment effect), we collected data on all patients receiving NPPV outside the study for the last 18 months of the study period. We compared the study patients to those receiving NPPV in terms of need for reintubation, duration of ventilation, length of ICU and hospital stay, ICU and hospital survival, and diagnoses. We also examined the recruitment rate and NPPV failure rate over time, which may also suggest a selection bias for patients within the study. All analyses were performed using SPSS Graduate Pack 9.0 (Evanston, Ill).

RESULTS

A total of 2763 patients were screened during the study period. Of these, 880 fulfilled the inclusion criteria of requiring ventilatory support for more than 48 hours or having underlying chronic cardiac or lung disease. Following application of the exclusion criteria, only 358 of these remained eligible (Figure). Of these 358 patients, 81 developed respiratory distress and were randomized (42 to standard therapy and 39 to noninvasive ventilation). The 2 study groups were similar in age, APACHE II score, duration of initial period of mechanical ventilation, time to respiratory distress after extubation, and diagnostic group (TABLE 1). Compliance with recording of the extubation criteria were variable: 76 patients had respiratory rate recorded, 75 had minute ventilation recorded, 54 had maximal inspiratory pressure recorded, and 45 had vital capacity recorded. Missing data were evenly distributed between the 2 study groups and summary data were similar (Table 1). On reviewing compliance with the extubation criteria, all patients had their reason for intubation reversed and were awake and afebrile. Of those with these measurements, all had a maximal negative pressure of at least –20 cm H_2O. More leeway was given for respiratory rate and vital capacity so that 10 of the 76 patients with a respiratory rate recorded had a rate greater than 25/min but none greater than 30/min. Only 6 of 45 patients with a recorded vital capacity had a value less than 600 mL, and only 1 of these had a respiratory rate of greater than 25/min. In summary, the extubation guidelines were generally well adhered to.

The rate of reintubation in the standard therapy group was 69% (TABLE 2), which was similar to the 65% we had estimated before the study. We found no difference between rates of reintubation: 72% in the NPPV group and 69% in the standard therapy group (relative risk [RR], 1.04; 95% confidence interval [CI], 0.78-1.38; Table 2). Although there was a trend toward a reduction in the time to reintubation for those patients being reintubated (P=.12), this was not statistically significant. In addition, although there was a trend toward a shorter duration of conventional mechanical ventilation in the NPPV group, this did not reach statistical significance (Table 2). There was no difference in the duration of ICU or hospital length of stay or ICU or hospital survival (31% for both groups; RR,

Table 1. Baseline Characteristics of the Study Group*

Characteristics	NPPV (n = 39)	Standard Therapy (n = 42)	*P* Value
Age, y	68.3 (13.1)	68.6 (12.4)	.93
APACHE II score	22.5 (7.1)	24.0 (7.9)	.38
Duration of initial ventilation, d			
Mean (SD)	3.8 (4.0)	5.0 (4.5)	.24
Median (range)	2 (0-19)	4 (0-21)	.16
Extubation criteria			
Vital capacity, L (n = 45)	1.10 (0.44)	0.92 (0.41)	.77
Peak negative inspiratory pressure, cm H_2O (n = 54)	35.2 (10.1)	34.4 (10.3)	.29
Respiratory rate, breaths/min (n = 76)	19.9 (5.0)	21.1 (4.6)	.74
Minute ventilation, L/min (n = 75)	9.7 (2.9)	9.5 (2.5)	.90
Time from extubation to respiratory distress, h	9.95 (10.1)	9.68 (10.1)	
At time of randomization			
Respiratory rate, breaths/min	31.8 (5.9)	31.2 (6.4)	.64
Heart rate, beats/min	109.1 (18.7)	108.9 (26.1)	.97
Mean arterial pressure, mm Hg	100.1 (21.6)	95.8 (18.4)	.34
pH	7.41 (0.08)	7.39 (0.09)	.22
Pa_{O_2}/F_{IO_2} ratio	142.6 (54.5)	156 (85.3)	.42
Pa_{CO_2}, mm Hg	48.4 (12.8)	50.9 (17.2)	.48
No. of Patients in Each Diagnostic Category			
Cardiac	16	12	
Respiratory			
COPD	3	6	
Others	8	10	
Vascular surgery	3	4	
Trauma	2	4	
Gastrointestinal tract	2	3	
Neurological	1	2	
Sepsis	3	0	
Renal	0	1	
Hematological	1	0	
Total	**39**	**42**	

*Data are presented as mean (SD) unless otherwise indicated. NPPV indicates noninvasive positive-pressure ventilation; APACHE II, Acute Physiology and Chronic Health Evaluation II; F_{IO_2}, fraction of inspired oxygen, and COPD, chronic obstructive pulmonary disease.

0.99; 95% CI, 0.52-1.91; Table 2). Pneumonia rates recorded by attending physicians were similar in both groups (Table 2).

Of the 39 patients randomized to receive NPPV, 10 did not tolerate this intervention and 8 of these were reintubated. There was no difference in reintubation rates for those patients who tolerated NPPV (20/29, 69%) compared with the rest (37/52, 71%) (efficacy analysis; $P=.499$; RR, 0.97; 95% CI, 0.72-1.31). Protocol violations occurred in both groups. Three patients in the NPPV did not receive it; 1 required intubation by the time the NPPV was available, and 2 did not receive it for unclear reasons (neither required intubation). Three patients in the standard treatment group received delayed NPPV as rescue therapy beyond the time of randomization despite developing worsening respiratory distress to the point that they met intubation criteria. One of these required intubation. The mean (SD) IPAP was 10.2 (2.0) cm H_2O, and the mean (SD) EPAP was 5.1 (1.2) cm H_2O. Patients wore NPPV on and off for a mean (SD) of 1.7 (1.2) days (range, 1-6 days) and a total of 12.3 (16.2) hours (range, 0-66 hours). There were 2 cases of pressure necrosis that developed in the NPPV group in patients who receive 37 and 42 hours of NPPV, respectively.

Post hoc, we explored the possibility that patients who presented with hypercapnic respiratory failure may benefit more than others from the use of NPPV when developing respiratory distress. Five patients did not have arterial blood gases recorded before randomization. Of the remaining 76 patients, 19 (11 control, 8 NPPV patients) had both a pH of less than 7.35 and a $PaCO_2$ of more than 45 mm Hg. In this subgroup, there was no difference in reintubation rate or hospital survival. Similarly, no differences were found in these outcomes in the nonhypercapnic group (of these 57 patients, only 10 had a PaO_2/FIO_2 ratio greater than 200).

Our analyses to determine whether there was a selection bias that led to the systematic exclusion of patients from the study who benefit from NPPV found no difference in rates of recruitment beyond an initial drop in the first year (29 to 20 non-COPD patients per year) and no difference in the relative success of NPPV over time. Finally, we identified 44 patients who fulfilled our inclusion criteria and received NPPV outside the study during the final 18 months of the study. Although these patients differ from our study population by not having our specific exclusion criteria applied (within the study, more than half of patients who met inclusion criteria were excluded), they represent a reasonable sample for this purpose. We found a trend toward a lower reintubation rate among the nonstudy patients (55% vs 70%, $P=.08$, TABLE 3). When we examined the distribution of patients across diagnostic groups, a greater proportion of patients in the nonstudy group with a cardiac disorder diagnosis appeared to exist compared with the study population. Thus, it is possible that a selection bias occurred during the study period. However, when one examines the more meaningful outcomes of survival and length of stay, there was no difference between study and nonstudy patients.

Table 2. Outcomes for the Study Groups*

Outcomes	NPPV (n = 39)	Standard Therapy (n = 42)	*P* Value
Reintubation, No. (%)	28 (72)	29 (69)	.79
Pneumonia, No. (%)	16 (41)	17 (40)	.61
Duration of ventilation†			
Mean (SD)	8.4 (7.4)	17.5 (28.0)	.11
Median (range)	6.7 (0.5-28.6)	8.9 (2.0-146.7)	.12
ICU length of stay			
Mean (SD)	15.1 (10.9)	19.4 (25.0)	.32
Median (range)	11.9 (3.6-41.7)	10.8 (2.3-152.7)	.72
Hospital length of stay			
Mean (SD)	32.2 (25.4)	29.8 (28.4)	.69
Median (range)	19 (6-111)	22 (4-162)	.51
ICU survival, No. (%)	33 (85)	32 (76)	.34
Hospital survival, No. (%)	27 (69)	29 (69)	.99

*NPPV indicates noninvasive positive pressure ventilation; ICU, intensive care unit.
†Duration of mechanical ventilation includes only time using conventional ventilator.

Table 3. Comparison of Study Group and Patients Using Noninvasive Positive Pressure Ventilation Outside Study*

Variable	Study Participants (n = 81)	Nonstudy Patients (n = 24)	*P* Value
Intubation, No. (%)	87 (70)	24 (44)	.08
Age, mean (SD), y	68.5 (13)	68.2 (15)	.92
APACHE II, mean (SD), score	23.3 (7.5)	21.5 (8.31)	.21
ICU length of stay, median (range), d	11 (2-153)	13.4 (4-46)	.60
Hospital length of stay, median (range), d	22 (4-351)	28.5 (6-76)	.19
ICU mortality, No. (%)	16 (20)	11 (25)	.50
Hospital mortality, No. (%)	25 (31)	15 (38)	.71

*APACHE II indicates Acute Physiology and Chronic Health Evaluation II; and ICU, intensive care unit.

COMMENT

Contrary to our expectations, we found no apparent benefit from the application of NPPV in patients who develop respiratory distress within the first 48 hours of extubation. Despite a trend toward a longer time to reintubation for patients with NPPV, the actual rates of reintubation did not differ between patients treated with or without NPPV. The ICU and hospital lengths of stay and hospital mortality did not differ. This randomized trial suggests that the routine use of NPPV for *all* patients who

develop respiratory distress after extubation is not effective.

The published literature addressing the use of NPPV to avoid postextubation intubation is sparse. Two randomized controlled trials have examined the use of NPPV in selected patients as an adjunct to weaning from mechanical ventilation. Nava et al[25] found that patients with an exacerbation of COPD who required intubation but were awake after 1 to 2 days benefited from early extubation (from high pressure support levels) to NPPV. Patients randomized to receive NPPV had a shorter duration of ventilatory support, a shorter length of stay, less pneumonia, and improved survival compared with those undergoing a conventional wean from mechanical ventilation.[25] Girault et al[26] conducted a similar study on a more heterogeneous population (not all with COPD) and after a variable period of conventional mechanical ventilation. These investigators found a decreased duration of conventional mechanical ventilation among patients randomized to early extubation to NPPV but no difference in other outcomes. Jiang et al[27] have reported the only randomized trial published to date that included patients who had NPPV applied directly after being weaned and extubated in a conventional manner from mechanical ventilation. They randomized all patients following planned or self-extubation to either NPPV or usual treatment and found no benefit from NPPV. Their patient group did include a surprisingly high proportion of patients who extubated themselves (40%). The literature describing the effect of NPPV to avoid reintubation in patients who develop respiratory distress some time following extubation, the focus of our study, consists of case series,[8,29] a study using historical controls,[30] and one randomized controlled trial available only in abstract format at the time of this writing.[31] Both uncontrolled case series[8,29] have suggested benefit from NPPV in a heterogeneous group of patients with respiratory failure, some of whom were recruited during the postextubation period. Hilbert et al[30] described a decreased rate of intubation compared with historical controls among COPD patients who developed respiratory distress after extubation who were treated with NPPV. A recent abstract of a randomized controlled trial suggested benefit among patients who underwent ventilatory support for at least 3 days, but this study has yet to undergo further peer review.[31] To date, to our knowledge, our study is the only randomized controlled trial published evaluating the use of NPPV among patients with postextubation respiratory distress. Our study differs from the 3 published randomized controlled trials in timing of application of NPPV because these studies assessed the effectiveness of NPPV use immediately following extubation (not waiting for patients to develop respiratory distress), either at a point when patients were weaning but still required ventilatory support[25-27] or when patients were considered fully weaned.[27] No benefit was demonstrated for our population of patients who either required 48 hours of mechanical ventilation or had underlying chronic respiratory or cardiac disease.

Studies of NPPV and similar technologies are difficult to blind. This lack of blinding of patients and clinicians may not be expected to attenuate the treatment effect of NPPV because the direction of this type of bias tends to favor the intervention group. We did not specify the use of cointerventions for the 2 treatment groups, leaving this up to the attending staff. This is a potential source of bias in our study because it is possible that patients were treated less aggressively with other therapies, such as diuretics or bronchodilators, in the NPPV group if the attending staff believed that NPPV would obviate their need. We did not record the relative use of these cointerventions, and medical management was otherwise at the discretion of the attending physicians.

The success of NPPV is clearly linked to the expertise and enthusiasm for its effectiveness among those using it. Centers with greater expertise may be more likely to report better outcomes. In our center, we had used NPPV for these patients for 1 year before the study and had frequent in-service training sessions to maintain expertise and enthusiasm among the respiratory therapists and physicians who applied NPPV. It is possible that other, more experienced centers may have achieved better results. The timing of the application of NPPV after extubation may affect outcome such that early use may be more beneficial. To test the effect of NPPV among patients with respiratory distress, we waited until these symptoms occurred. Earlier application could yield different results.

In this randomized trial, we attempted to enroll a higher-risk group of patients with either premorbid cardiac or respiratory disease or who had required at least 2 days of ventilatory support. Although it is clear that applying NPPV to all patients who fit this description is not beneficial, there may be a specific subgroup in this heterogeneous population who could benefit from this treatment. Patients with COPD were excluded after 1 year because we did not believe that it was ethical to continue to randomize them due to strong established literature supporting the use of NPPV for COPD exacerbations. We also were concerned that physicians may have systematically kept patients out of the study who could potentially benefit from NPPV. Although we did find a nonsignificant trend toward a decreased reintubation rate among those patients receiving NPPV outside the study, these patients were not directly comparable to our study patients because they met inclusion but not exclusion criteria. In addition, although there was a trend toward a decreased rate of reintubation, the more important outcomes of length of stay and survival were no different.

Based on this randomized trial, we cannot recommend the routine use of NPPV for patients who require mechanical ventilatory support for more than 48 hours or those with a known history of cardiac or non-COPD respiratory disease who develop respiratory distress within 48 hours of extubation. Although it is clear that applying

NPPV to all patients who fit this description is not beneficial, there may be a subgroup who could benefit that we could not detect within this heterogeneous population. We found no difference in the need for reintubation, length of stay, or mortality. Our study is consistent with prior literature suggesting that if NPPV is to be used after extubation, it might be most effective if applied early, before the development of respiratory distress. However, further work is required to clarify which patients, if any, may benefit from the use of NPPV in this setting.

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Acquisition of data: Powers, Block.
Analysis and interpretation of data: Keenan.
Drafting of the manuscript: Keenan, Block.
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Statistical expertise: Keenan.
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