Noninvasive positive-pressure ventilation in acute respiratory failure outside clinical trials: Experience at the Massachusetts General Hospital*

Guilherme Schettino, MD, PhD; Neila Altobelli, BA, RRT; Robert M. Kacmarek, PhD, RRT

Background: **Noninvasive positive-pressure ventilation (NPPV) has been shown to be effective in select patients enrolled in clinical trials. However, few data are available on the use of NPPV as routine standard medical care for patients with respiratory failure outside of controlled trials.**

Measurements and Main Results: **All patients receiving NPPV for a 1-yr period for acute or acute on chronic respiratory failure who did not select do not intubate/resuscitate status were evaluated. Demographic, physiological, and laboratory data were collected for as long as NPPV was provided. Data were recorded on 449 patients. Intubation rate was 18%, 24%, 38%, 40%, and 60%, respectively, for patients with cardiogenic pulmonary edema (n = 97), acute exacerbation of chronic obstructive pulmonary disease (n = 87), non-chronic obstructive pulmonary disease acute hypercapnic respiratory failure (n = 35), postextubation respiratory failure patients (n = 95), and acute hypoxemic respiratory failure (n = 144). The hospital mortality for patients with acute hypoxemic respiratory failure who failed NPPV was 64%. A logistic regression showed that baseline Simplified Acute Physiology Score II (odds ratio [OR], 1.07; 95% confidence interval [CI], 1.05–1.10; $p < .0001$), Glasgow Coma Scale (OR, 0.76; 95% CI, 0.66–0.87; $p < .0001$), Pao_2/Fio_2 ratio (OR, 0.98; 95% CI, 0.93–0.99; $p = .02$), and serum albumin (OR, 0.30; 95% CI, 0.16–0.57; $p < .001$) were the variables associated with NPPV failure.**

Conclusion: **NPPV as routine standard medical care resulted in the intubation of a similar percentage of patients with respiratory failure due to cardiogenic pulmonary edema and chronic obstructive pulmonary disease exacerbation as shown in randomized controlled trials but in a higher percent of patients with hypoxemic respiratory failure than reported in these trials. NPPV failure was associated with high hospital mortality for patients with hypoxemic respiratory failure. (Crit Care Med 2008; 36:441–447)**

KEY WORDS: noninvasive positive-pressure ventilation; respiratory failure; chronic obstructive pulmonary disease; cardiogenic pulmonary edema; hypoxemic respiratory failure

Noninvasive positive-pressure ventilation (NPPV) has become an integral part of ventilatory support to critically ill patients since initial reports appeared in the literature in the late 1980s (1, 2). Today, numerous randomized controlled trials support the use of NPPV in many specific clinical settings (3–16). NPPV has become the standard of care for the management of chronic obstructive pulmonary disease (COPD) patients in an acute exacerbation (3–6), and NNPV also is considered first-line therapy for the management of patients with acute cardiogenic pulmonary edema (7–10). NPPV is useful in the transition from invasive mechanical ventilation to spontaneous breathing for patients with COPD (11, 12) or patients at high risk for reintubation (13, 14). In spite of the controversy surrounding the use of noninvasive ventilatory support in acute hypoxemic respiratory failure (17), NPPV has demonstrated its usefulness in patients who are immunosuppressed (18), in patients following solid organ transplantation (19), in post–lung resection patients (20), and in general populations of patients with acute hypoxemic respiratory failure (21, 22).

Contrary to the impressive list of positive randomized controlled trials on the use of NPPV, minimal data exist in the literature defining the outcomes from daily routine standard use of NPPV (23–25). In addition, some institutions rarely use NPPV as first-line therapy in acute respiratory failure.

We at the Massachusetts General Hospital have been using NPPV to manage acute respiratory failure since the early 1990s and currently ~25% of our patients requiring some form of ventilatory support receive it noninvasively. We questioned if our results were consistent with those described in randomized controlled trials. Based on our experience with NPPV, we hypothesized that we would be able to match the results demonstrated in the clinical trial literature. We present data for a full calendar year defining the Massachusetts General Hospital's experience with the clinical use of NPPV.

METHODS

The Massachusetts General Hospital subcommittee for human research approved the study protocol and waived the need for consent. The following description of the methods was previously published in *Critical Care Med-*

***See also p. 630.**

From the Harvard Medical School (GS, RMK) and Massachusetts General Hospital (GS, NA, RMK), Boston, MA.

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For information regarding this article, E-mail: rkacmarek@partners.org

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icine (26) and is reproduced here with minor modification with permission.

Study Design. Between January 1 and December 31, 2001, we conducted a prospective observational study of all patients receiving NPPV at the Massachusetts General Hospital, in Boston, MA. In this publication, we report only the data on those adult patients (>18 yrs) who received NPPV for the first time for acute respiratory failure. The data for patients whose status was do not intubate has been published previously (26). In the context of this study, NPPV is defined as either mask continuous positive airway pressure (CPAP) or mask pressure support ventilation with positive end-expiratory pressure (PEEP). In all cases, NPPV was managed by the patient's primary physician, which was any licensed physician at the Massachusetts General Hospital; the use of NPPV did not require a pulmonary and intensivist consult. NPPV was used to manage acute or acute on chronic respiratory failure in patients never receiving NPPV before the current admission. Avoidance of intubation was the criteria used to define successful application of NPPV.

When NPPV was ordered, the respiratory therapist assigned to the care of the patient recorded data regarding patient location (emergency room, intensive care unit [ICU], or regular medical/surgical unit), time of NPPV initiation, physiological parameters (respiratory rate, heart rate, temperature, arterial blood pressure), neurological status (Glasgow Coma Scale [GCS]), and (when available) arterial blood gases immediately before NPPV initiation (baseline data). After an initial period of stabilization, within 2 hrs of the start of NPPV, the ventilator settings, mask type, and any complication related to NPPV were recorded along with physiological parameters and neurological status. As long as the patient received NPPV, data related to NPPV application, patient tolerance, and complications associated with NPPV were recorded at 6 am and 6 pm. This was recorded by the therapist caring for the patient for the previous 11 hrs and documented the issues and data during that time period. Demographic data, medical diagnosis, and laboratory results were extracted from the patient's electronic chart. The final hospital outcome was obtained from the medical discharge summary.

A modified Simplified Acute Physiological Score (SAPS) II was calculated with the data obtained immediately before NPPV initiation (26). Given that SAPS II was calculated at a specific point in time and not from data over a 24-hr period, urinary output was not included in the calculation.

The etiology of respiratory failure was defined based primarily on the medical diagnosis, laboratory and radiological findings, and (when available) arterial blood gases. Patients were classified into five groups as follows (26): a) acute exacerbation of chronic obstructive pulmonary disease; b) acute or acute on chronic hypercapnic respiratory failure in patients without COPD; c) acute hypoxemic respiratory failure (Pao_2/Fio_2, <300 mm Hg and normal acid base status); d) acute cardiogenic pulmonary edema in patients with the diagnosis of acute or chronic heart failure; and e) postextubation acute respiratory failure, defined as the need for NPPV within 48 hrs after extubation.

Patients were considered weaned from NPPV 72 hrs after its discontinuation, or at the time of hospital discharge.

Application of NPPV. During initiation of NPPV, ventilator settings were gradually increased over time as the patients tolerated the application. When the mask was first applied to the patient's face, it was held by the patient or the therapist until the patient accepted the application. PEEP was begun at the lowest setting possible and ventilating pressures were set at 3–5 cm H_2O to allow the patient to slowly acclimate to the application of NPPV. As the patient became more comfortable with the application of NPPV, the pressures were gradually increased to establish an acceptable ventilatory pattern (tidal volume >300 mL, respiratory rate <30 breaths/min) and the mask was strapped onto the patient's face. PEEP levels generally were set between 5–10 cm H_2O and ventilatory pressure about 10–15 cm H_2O. Peak airway pressures were maintained ≤20 cm H_2O. If there was reddening on the bridge of the nose with the application of NPPV, DuoDerm was applied to the patient's nose.

Data and Quality Assurance. This study was an observational data collection, and the investigators did not influence any aspect of patient care. Before initiation, the data recording forms were discussed with all respiratory therapists involved in data collection. All aspects of the GCS were discussed in detail. Assurance of consistent scoring was made by providing examples and comparing ratings among staff obtaining this data. Every month, one of the investigators met with the entire respiratory therapist team to discuss the study progress, reinforce the appropriate completion of data collection forms, and discuss the components of the GCS. Completion of data collection forms was monitored daily by comparing the forms received with the respiratory care department summary of patients on service receiving NPPV. Of the daily forms, 5% were reviewed in detail ensuring that data listed was correctly recorded by reviewing the medical record and interacting with the therapist completing the form.

Data Analysis. The primary end point evaluated was need for endotracheal intubation. Continuous variables (age, SAPS II, GCS, physiological variables, and laboratory tests) were compared with unpaired Student's *t*-tests and categorical data were compared using Fisher's exact test. All continuous variables that showed a $p < .1$ in the univariate analysis were entered in a logistic regression analysis to identify the predictors of need for intubation immediately before NPPV and within 2 hrs of NPPV initiation. Variables with a $p < .05$ were considered significant and reported as odds ratio (OR) with 95% upper and lower confidence intervals (CI). All statistical analysis was performed with SPSS version 9.0 (SPSS, Chicago, IL).

RESULTS

NPPV was used to manage 458 episodes of acute respiratory failure in 449 patients over the 12-month study period. In nine patients, NPPV was used twice during a single admission. The average age of the patients treated was 66.4 ± 15.5 yrs and 51% were female. NPPV was initiated 47% of the time in an ICU, 33% of the time on general medical-surgical units, and 20% of the time in the emergency ward (EW). After initial stabilization, 53% of patients were managed in the ICU and 35.3% were managed on the general medical surgical units. The remaining 11.6% were managed exclusively in the EW. During ongoing management of these patients, the therapist-to-patient ratio for both noninvasive and invasive ventilatory support averaged 1:6 to 1:8 and the nurse to patient ratios were about 1:2 in the ICU and 1:4 to 1:6 outside the ICU. Overall, NPPV prevented intubation in 62.6% (n = 282) of these acute applications. Successful application (avoidance of intubation) of NPPV in our patients was highly predictive of hospital survival. Only 5.4% of those successfully managed with NPPV died vs. 46.6% of those failing NPPV and requiring intubation ($p < .001$). Overall mortality was 21.2%. In general, patients managed solely in the EW had the best outcome. Only 22.6% were intubated, and the mortality of EW-managed patients was 7.5%. Patients managed in the ICU had the worst outcome; 49.4% of the ICU-managed patients were intubated and 28.4% died. Patients on the general wards were intubated at a 27.3% rate and 14.9% died. The majority of patients exclusively managed in the EW were patients with cardiogenic pulmonary edema.

Figure 1 shows the distribution of patients into five categories along with the percent intubated and the percent of those intubated who died. Intubation rate was low in patients with cardiogenic pulmonary edema (18%) and COPD exacerbation (24%); however, mortality of those intubated was high (39% and 33%, respectively). The intubation rate, however, for patients with hypoxemic respiratory failure was 60% and 64% of those intu-

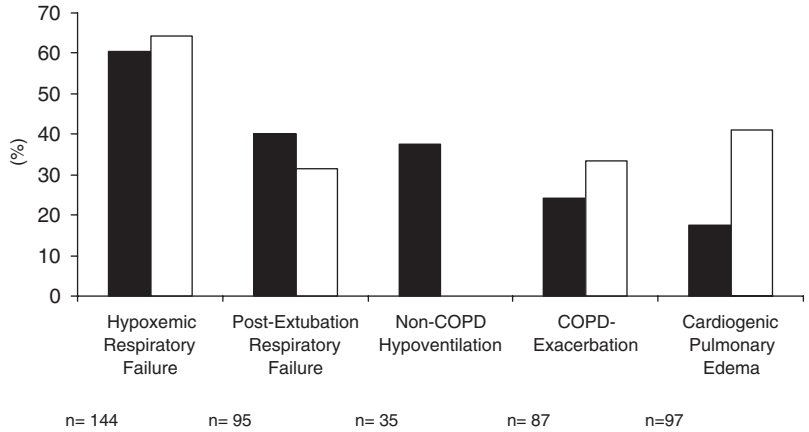

Figure 1. Number of patients, percent needing intubation (*black bars*), and percent of those intubated who died (*white bars*) are presented for patients with acute hypoxemic respiratory failure, postextubation respiratory failure, non–chronic obstructive pulmonary disease (*COPD*) hypercapnic respiratory failure, COPD exacerbation, and cardiogenic pulmonary edema.

Table 1. Physiologic and laboratory data at baseline and 2 hrs after noninvasive positive-pressure ventilation (NPPV) initiation of all patients receiving NPPV

	Success (n = 282)	Failure (n = 176)	Univariate Analysis *p* Value	Logistic Regression OR (95% CI) *p* Value
Age, yrs	66.3 ± 15.8	66.6 ± 15.0	NS	
Baseline				
SAPS II	31.7 ± 10.1	39.9 ± 11.4	<.001	1.07 (1.05–1.10) <.001
Glasgow Coma Scale	14.1 ± 1.9	12.6 ± 3.2	<.001	0.76 (0.66–0.87) <.001
Respiratory rate, min	29.1 ± 10.5	29.7 ± 8.9	NS	
Heart rate, min	98.1 ± 23.6	102.8 ± 22.2	NS	
Pao_2/Fio_2[a]	200 ± 98	163 ± 87	<.001	0.98 (0.93–0.99) .02
$Paco_2$, mm Hg[a]	60.8 ± 21.5	56.6 ± 23.1	NS	
pH[a]	7.33 ± 0.10	7.31 ± 0.11	NS	
NPPV 2 hrs				
SAPS II	29.2 ± 9.6	38.8 ± 11.7	<.001	1.08 (1.05–1.10) <.001
Glasgow Coma Scale	14.4 ± 1.45	12.7 ± 3.16	<.001	0.62 (0.52–0.73) <.001
Respiratory rate, min	23.6 ± 7.5	26.6 ± 9.7	.001	
Heart rate, min	90.1 ± 19.6	97.4 ± 23.6	.001	1.02 (1.0–1.03 .02
Pao_2/Fio_2[b]	237 ± 102	186 ± 100	<.001	0.99 (0.98–0.99) .02
$Paco_2$, mm Hg[b]	52.4 ± 16.9	50.8 ± 18.1	NS	
pH[b]	7.36 ± 0.22	7.36 ± 0.10	NS	
Laboratory				
Hematocrit, %	34.4 ± 6.5	32.1 ± 6.0	.001	
White cell count (×1000)	13.1 ± 6.3	16.1 ± 12.7	.001	
Urea, mg/dL	31.2 ± 22.8	38.8 ± 31.04	.003	
Albumin, g/dL[c]	2.89 ± 0.65	2.39 ± 0.63	<.001	0.30 (0.16–0.57) <.001

OR, odds ratio; CI, confidence interval; SAPS, Simplified Acute Physiology Score; NS, not significant.

[a]Data available for 330 cases; [b]332 cases; [c]390 cases.

bated died. The intubation rate for non-COPD acute hypercapnic respiratory failure was 38% and 40% for postextubation respiratory failure. Most patients failing NPPV in all groups were intubated within 24 hrs (62%) after starting NPPV; however, 25% of patients were intubated after 48 hrs.

Table 1 presents clinical and laboratory findings before and 2 hrs after initiation of NPPV for the total population of patients. Before initiation of NPPV, those successfully managed with NPPV had a significantly lower SAPS II score, white cell count, and blood urea level, and a higher GCS, Pao_2/Fio_2, hematocrit, and serum albumin level. After 2 hrs of NPPV, those successfully managed with NPPV had a significantly lower SAPS II score, respiratory rate, and heart rate, and a higher GCS and Pao_2/Fio_2. A logistic regression analysis showed that SAPS II score (OR, 1.07; 95% CI, 1.05–1.10; $p < .0001$), GCS (OR, 0.76; 95% CI, 0.66–0.87; $p < .0001$), Pao_2/Fio_2 (OR, 0.98; 95% CI, 0.93–0.99; $p = .02$), and serum albumin (OR, 0.30; 95% CI, 0.16–0.57; $p < .001$) recorded before or at 2 hrs of NPPV were predictive of NPPV failure. Table 2 presents the data from patients with acute hypoxemic respiratory failure. In this group of patients, SAPS II and serum albumin recorded at baseline, as well as SAPS II, GCS, and Pao_2/Fio_2 ratio recorded within 2 hrs of NPPV, were the variables associated with NPPV failure.

The reason for intubation of patients in each of the five diagnostic categories is presented in Table 3. By far, refractory hypoxemia was the most common cause for intubation (30.1%; n = 53), followed by depressed mental status (15.3%; n = 27), and respiratory acidosis (14.2%; n = 25). In addition, 9% (n = 16) of intubations were because of a cardiorespiratory arrest or impending arrest. Only 2% (n = 2) were because of vomiting and an additional 2% (n = 2) because of mask intolerance.

Table 4 lists the mode of ventilatory support, the PEEP/CPAP and pressure support levels used, and the Fio_2 set for all five diagnostic categories at the initiation of NPPV and Figure 2 shows the distribution of ventilator types used. Facial (93%) and nasal (7%) masks were the interfaces used by these patients.

DISCUSSION

The primary findings of this study can be summarized as follows: a) except for the management of acute hypoxemic respiratory failure, NPPV can be safely applied in a large university hospital with the same successful avoidance of intubation as demonstrated in randomized controlled trials; b) the management of acute hypoxemic respiratory failure could not be performed successfully, because a high percent of these patients failed NPPV and a high percentage of those intubated died; c) SAPS II, GCS, Pao_2/Fio_2 ratio, and serum albumin were the only variables predicting NPPV failure; and d) side effects associated with the use of NPPV were minimal.

Keys to Successful Application of NPPV. Part of the reason for our successful application of NPPV, we speculate, has been the training of the respiratory care staff administering NPPV and the orientation of the nursing staff caring for these patients. All respiratory care staff attended a 4-hr training session in which indications, equipment, and techniques

for initial application of NPPV are discussed and demonstrated. In addition, all staff members applied NPPV to each other to identify the issues that increased the likelihood of success and the correct mask type and size, to experience initiation with very low ventilating pressures and a gradual increase in pressure as the patient adjusts to NPPV, to learn to provide education to the patient regarding the goals of therapy, and to experience the need to spend time (1–2 hrs) at the bedside during initiation of therapy. All nursing personnel receive classroom orientation to NPPV and bedside instruction by the therapist during application of NPPV. As noted in Figure 2, NPPV is applied almost exclusively with devices designed for this purpose, and a large variety of masks of different sizes and types are available. A critical aspect of training is to ensure a correctly sized mask is used, that being the smallest size fitting the patient's face.

Respiratory Failure Diagnosis and Outcome. Our outcomes from the application of NPPV in acute exacerbation of COPD and acute cardiogenic pulmonary edema were consistent with recent literature (3–10). Meta-analysis (27) suggests that the use of NPPV in patients with an acute exacerbation of COPD, particularly in those with a severe exacerbation, decreases intubation rate, length of invasive ventilatory support, length of hospital stay, hospital-acquired infection, and mortality. The use of NPPV in cardiogenic pulmonary edema is more complex; however, it is very well supported by clinical trials (7–10) and systematic reviews (28). Data from the late 1980s (7) clearly supports the use of CPAP in acute cardiogenic pulmonary edema characterized by hypoxemia. However, recent trials (9–10) also support the use of pressure support ventilation with PEEP in patients who present with hypercarbia. Of note is the trial by Dr. Mehta and colleagues (8) that observed a higher incidence of myocardial infarction in a small group of patients (12 vs. 13) managed with pressure support ventilation with PEEP when compared with CPAP. We, however, had no reports of increased ischemia as a result of noninvasive ventilation in this group of patients.

Our outcome for the use of NPPV in postextubation respiratory failure was only moderately successful. A large number of trials have now focused on the use of NPPV in weaning failure (11–14, 29–31). These trials identify a number of settings where NPPV should and should not be used during weaning. Use in patients with COPD appears to be indicated regardless of the circumstances (11, 29–31). NPPV is able to successfully support COPD patients failing weaning trials who are extubated (11, 29). NPPV appears most indicated in patients who success-

Table 2. Physiologic and laboratory data at baseline and 2 hrs after noninvasive positive pressure ventilation initiation on patients with acute hypoxemic respiratory failure

	Success (n = 57)	Failure (n = 87)	Univariate Analysis *p* Value	Logistic Regression OR (95% CI) *p* Value
Age, yrs	60.5 ± 18.7	65.0 ± 15.6	NS	
Baseline				
SAPS II	31.4 ± 14.5	42.6 ± 11.6	<.001	1.07 (1.03–1.11) <.001
Glasgow Coma Scale	14.1 ± 2.3	12.7 ± 3.3	.008	
Respiratory rate, min	31.6 ± 11.6	31.8 ± 8.7		
Heart rate, min	105.3 ± 17.5	107.3 ± 22.0		
Pao_2/Fio_2	164.4 ± 92.3	130.2 ± 74.8	.05	
$Paco_2$, mm Hg	50.7 ± 13.7	48.2 ± 17.7		
pH	7.38 ± 0.08	7.35 ± 0.12		
NPPV 2 hrs				
SAPS II	28.2 ± 12.3	41.8 ± 12.4	<.001	1.09 (1.05–1.13) <.001
Glasgow Coma Scale	14.4 ± 1.6	12.7 ± 3.4	.01	0.56 (0.38–0.82) .003
Respiratory rate, min	24.8 ± 8.1	28.0 ± 9.5	.04	
Heart rate, min	98.8 ± 19.6	102.8 ± 23.5		
Pao_2/Fio_2	212 ± 102	152 ± 87	.002	0.99 (0.98–0.99) .01
$Paco_2$, mm Hg	47.0 ± 12.5	45.5 ± 15.1		
pH	7.39 ± 0.07	7.36 ± 0.10		
Laboratory				
Hematocrit, %	34.0 ± 8.6	31.7 ± 5.5		
White cell count (×1000)	14.6 ± 8.8	15.9 ± 10.6		
Urea, mg/dL	26.2 ± 20.0	42.0 ± 33.8	.002	
Albumin, g/dL	2.6 ± 0.7	2.2 ± 0.6	.001	0.43 (0.21–0.89) .02

OR, odds ratio; CI, confidence interval; SAPS, Simplified Acute Physiology Score; NS, not significant.

Table 3. Primary reason for intubation for patients in each of the five diagnosis categories

No. of Patients	COPD Exacerbation (n = 87)	Non-COPD Hypercapnic Respiratory Failure (n = 35)	Acute Hypoxemic Respiratory Failure (n = 144)	Cardiogenic Pulmonary Edema (n = 97)	Postextubation Respiratory Failure (n = 95)
Mask intolerance			1	1	
Refractory hypoxemia	1		43	1	17
Refractory respiratory acidosis	8	4	8	1	4
Depressed mental status	5	5	11	1	5
Secretion accumulation			2		
Vomiting/aspiration			1		1
Severe arrhythmia			2	1	1
Hemodynamic instability			7	3	1
Cardiorespiratory arrest or risk for arrest	4	3	2	3	4
Surgical procedure	1		5	4	
Other/unknown	2	1	5	2	5
Total, *n*	21	13	87	17	38
Intubation rate, %	24	37	60	18	40

COPD, chronic obstructive pulmonary disease.

Table 4. Ventilatory mode and setting on all patients receiving noninvasive positive pressure ventilation

	Mode		Settings		
	PS/PEEP, %	CPAP, %	PEEP/CPAP, cm H_2O	PS, cm H_2O	FIO_2
COPD exacerbation (n = 87)	100	—	5.4 ± 1.0	13.2 ± 2.8	0.35 ± 0.16
Non-COPD hypercapnic respiratory failure (n = 35)	87	13	5.9 ± 1.1	13.7 ± 4.4	0.32 ± 0.12
Hypoxemic respiratory failure (n = 144)	66	34	6.1 ± 1.6	14.5 ± 4.1	0.58 ± 0.29
Cardiogenic pulmonary edema (n = 97)	40	60	6.6 ± 2.1	12.9 ± 4.4	0.61 ± 0.27
Postextubation respiratory failure (n = 95)	53	47	5.7 ± 1.6	14.9 ± 4.1	0.46 ± 0.24

PS, pressure support; PEEP, positive end-expiratory pressure; CPAP, continuous positive airway pressure; FIO_2, inspiratory oxygen fraction; COPD, chronic obstructive pulmonary disease.

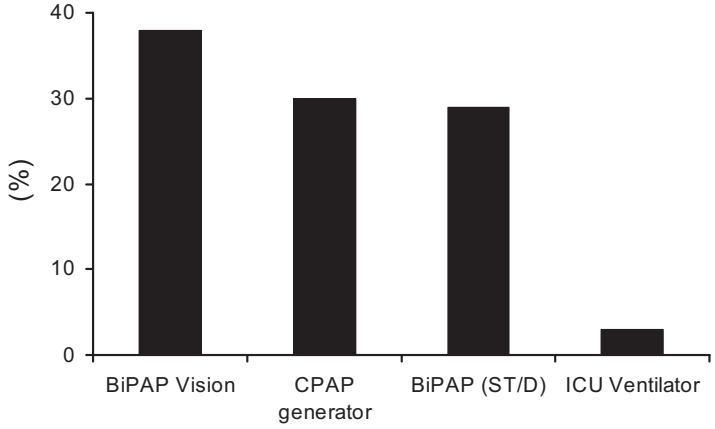

Figure 2. Distribution of the ventilators used. BiPAP Vision and BiPAP ST/D (Respironics, Carlsbad, CA) are ventilators designed for noninvasive positive-pressure ventilation. CPAP, continuous positive airway pressure; ICU, intensive care unit.

fully pass a spontaneous breathing trial and are extubated, but are at high risk for postextubation failure (13, 14). Specifically, in this setting NPPV seems useful in transitioning patients with COPD or cardiogenic pulmonary edema, patients with secretions problems, patients >65 yrs of age, and patients with comorbidities to unassisted spontaneous breathing (13, 14). However, the use of NPPV in postextubation failure seems particularly problematic in patients who develop hypoxemic respiratory failure (30). At the time that we gathered our data, we did not clearly define the circumstances when NPPV was applied postextubation; as a result, we are not able to specifically compare our data to these trials.

In our series, 35 patients without the diagnosis of COPD used NPPV to treat hypercapnic respiratory failure. This group of patients is more difficult to make comparisons with because there are no randomized controlled trials comparing NPPV to standard care in non-COPD hypoventilation. Most of these patients had ischemic stroke, degenerative neurological or neuromuscular disease, or decreased respiratory drive because of the use of medical or illicit drugs. In this group, depressed mental status was the most common reason for intubation. This is a group where the application of NPPV needs to be studied in a more systematic manner. We found NPPV particularly useful in patients with degenerative neuromuscular or neurological diseases. Well-defined randomized control trials are needed to more clearly define the role of NPPV in these patients.

The largest group of patients treated with NPPV, those with acute hypoxemic respiratory failure, did the least well, even though some of them had a relatively mild condition (Table 2). This increases our concern regarding the use of NPPV in this group. Our data are consistent with survey data reported by Dr. Antonelli and colleagues (32), but it is inconsistent with much of the published randomized controlled trials of NPPV in hypoxemic acute respiratory failure (21, 22). In the settings of immunosuppression (18), patients post–solid organ transplantation (19), and patients post–lung resection (20), the use of NPPV seems useful and beneficial and we would support its use. However, our experience contradicts the results of randomized controlled trials in patients with general causes of acute hypoxemic respiratory failure (21, 22). A potential reason for our high failure rate was the use of only moderate PEEP levels (Table 4). A more aggressive use of PEEP, and potentially a greater reliance on pressure support ventilation with PEEP as opposed to CPAP, may have improved our success rate.

Location and Outcome. Patients receiving NPPV were managed in three locations: in the ICU, on general medical/surgical wards, or in the EW. It is important to note that the differences in outcome (intubation and death) by location reflect that the majority of patients managed solely in the EW presented with cardiogenic pulmonary edema. If they were not intubated and sent to an ICU, or did not die quickly in the EW, the course of NPPV was rather short, in many cases mere hours. Patients who were managed in the ICU were generally the sickest of the patients maintained on NPPV. Patients from the medical/surgical wards or the EW that were maintained on the wards, as opposed to the ICU, were generally those requiring less monitoring and who were capable of periods >1 hr independent of NPPV. Patients maintained in the ICU generally required greater overall support, frequently requiring continuous NPPV, at least initially. However, we did not and do not have absolute criteria defining if a patient will be managed in the ICU or on the general medical/surgical wards.

Causes of Failure and Complications. When all patients were grouped together, SAPS II, GCS, and Pa_{O_2}/FIO_2 ratio recorded before NPPV initiation (baseline) or within 2 hrs of noninvasive ventilation were associated with NPPV success. These data are consistent with several studies published in the last decade (23, 25, 33). In addition, serum albumin recorded within the first day of noninvasive

ventilation also was a good predictor for NPPV outcome. Our data did not identify a change in pH after the application of NPPV as a predictor of success. Part of this failure may be because of the lack of available blood gas data. Of the 458 cases of NPPV presented, blood gases before initiation were available in 330 cases and at 2 hrs from only 332 cases. In addition, many of the blood gases could not be matched before and 2 hrs after to the same patient. As a result, we may have missed relationships that were identified by others when specific interventions were designed into their studies. Also, failure of NPPV did not necessarily occur at the 2-hr time interval. Patients failed NPPV over the full course of its application, although most patients (62%) failed within the first 24 hrs of NPPV and 25% failed after 48 hrs of NPPV. We did not have blood gas data obtained at the time of NPPV failure. Finally, there was no specific definition identifying NPPV failure. The decision to intubate was determined individually by the medical team caring for the patient.

The primary cause of NPPV failure was refractory hypoxemia. However, the only groups in which this represented a large number of reintubations were those with hypoxemic respiratory failure and postextubation failure (Table 3). The second most common cause of NPPV failure was depressed mental status, and the third was refractory respiratory acidosis. Of concern were the 16 patients intubated because of a cardiorespiratory arrest or impending arrest. In a large series of patients with hypoxemic respiratory failure that were treated with CPAP, Dr. Delclaux and colleagues (33) pointed out that using NPPV could delay invasive ventilation and put patients at risk of cardiorespiratory arrest.

Our data are consistent with that published by other groups evaluating the application of NPPV in general clinical practice (23–25). Our ability to manage COPD and cardiogenic pulmonary edema patients with NPPV is consistent with that reported by these groups. However, the number of our patients with hypoxemic respiratory failure was a large proportion of the total group receiving NPPV, generally larger than those in other reports. But our outcome in these patients is similar if we separate cardiogenic pulmonary edema patients from those with other causes of hypoxemia respiratory failure.

The level of side effects experienced by patients was limited. Of 459 episodes of NPPV, only 2 patients were intubated because of vomiting/aspiration, a clear reflection of the safety of NPPV. We rarely increased peak airway pressure over 20 cm H_2O and even more rarely placed nasogastric tubes for gastric distension. Mask intolerance only resulted in two patients needing intubation, even though 93% of the time a full-face mask was used. Nasal ulcerations did occur, but were not considered a major problem. We believe this was a result of careful selection of a correctly fitting mask and the use of DuoDerm on the nose.

Limitations. The most important limitation of this study is the fact that it was not a randomized controlled trial. As a result, our success may have been a result of selecting patients with little need for ventilatory support. However, the consistency of our data with that in the published literature and our poor outcome in acute hypoxemic respiratory failure patients speak against this. In addition, we did not use a single ventilator or mask type, nor did we have specific protocols guiding the application of NPPV. Both may have compromised our results. Finally, we are a center with a great deal of experience in the application of NPPV, as a result our data may not be representative of the application of NPPV in centers with less experience.

CONCLUSION

Except for the management of acute hypoxemic respiratory failure, NPPV can be applied in clinical practice with the same intubation rate as in randomized controlled clinical trials. Side effects associated with NPPV are minimal.

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