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Effects of noninvasive positive pressure ventilatory support in non-COPD patients with acute respiratory insufficiency after early extubation

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Abstract *Objective:* To investigate the effects of noninvasive positive pressure ventilation (NPPV) on pulmonary gas exchange, breathing pattern, intrapulmonary shunt fraction, oxygen consumption, and resting energy expenditure in patients with persistent acute respiratory failure but without chronic obstructive pulmonary disease (COPD) after early extubation.
Design: Prospective study.
Setting: Multidisciplinary intensive care unit of a university hospital.
Patients: 15 patients after prolonged mechanical ventilation (> 72 h) with acute respiratory insufficiency after early extubation.
Interventions: Criteria for early extubation were arterial oxygen tension (PaO_2) ≥ 40 mm Hg (fractional inspired oxygen 0.21), arterial carbon dioxide tension ($PaCO_2$) ≤ 55 mm Hg, pH > 7.32, respiratory rate ≤ 40 breaths per min, tidal volume (V_T) ≥ 3 ml/kg, rapid shallow breathing index ≤ 190 and negative inspiratory force ≥ 20 cmH_2O. After extubation, two modes of NPPV were applied [continuous positive airway pressure (CPAP) of 5 cmH_2O and pressure support ventilation (PSV) with 15 cmH_2O pressure support].
Measurements and main results: Oxygenation and ventilatory parameters improved during both modes of NPPV ($p < 0.05$): increase in PaO_2 of 11 mm Hg during CPAP and 21 mm Hg during PSV; decrease in intrapulmonary shunt fraction of 7 % during CPAP and 12 % during PSV; increase in tidal volume of 1 ml/kg during CPAP and 4 ml/kg during PSV; decrease in respiratory rate 6 breaths/min during CPAP and 9 breaths/min during PSV. Oxygen consumption (15 % during CPAP, 22 % during PSV) and resting energy expenditure (12 % during CPAP, 20 % during PSV) were reduced ($p < 0.05$). $PaCO_2$ decreased, whereas minute ventilation and pH increased during PSV ($p < 0.05$). The median duration of NPPV was 2 days. Two patients had to be reintubated.
Conclusions: In non-COPD patients with persistent acute respiratory failure after early extubation, NPPV improved pulmonary gas exchange and breathing pattern, decreased intrapulmonary shunt fraction, and reduced the work of breathing.

Key words Noninvasive mechanical ventilation · Pressure support ventilation · Continuous positive airways pressure · Weaning criteria · Respiratory failure

Table 1 Characteristics of the study population at baseline (*APACHE* Acute Physiology and Chronic Health Evaluation, *FVC* forced vital capacity, *FEV_1* forced expiratory volume in IS, *Lung-TX* lung transplant, *Liver-TX* liver transplant)

Patient	Diagnosis[a]	APACHE II	Age (years)	Body weight (kg)	Duration of Ventilation (days)	FVC (l)	FEV_1/FVC (%)
1	Lung-TX	19	47	63	3	0.39	63
2	Lung-TX	18	34	67	6	0.45	67
3	Liver-TX	19	43	74	7	0.88	74
4	Lung-TX	20	43	78	6	0.41	69
5	Pneumonia	23	70	76	10	0.90	89
6	Lung-TX	17	40	56	8	0.58	78
7	Liver-TX	23	47	58	8	0.72	92
8	Lung-TX	18	39	71	4	0.39	78
9	Thoracic-trauma	22	65	77	7	0.83	89
10	Liver-TX	18	34	61	14	0.69	86
11	Lung-TX	20	35	55	6	0.57	79
12	Lung-TX	21	41	53	9	0.48	77
13	Peritonitis	24	63	73	10	0.85	89
14	Lung-TX	20	36	60	8	0.78	75
15	Heart failure	25	65	63	60	0.67	81
	Mean ± SD	20 ± 3	47 ± 12	65 ± 8	8.00 (6/10)[b]	0.64 ± 0.18	79 ± 8

[a] Lung-TX was carried out because of fibrosis
[b] Median (25^{th}/75^{th} percentiles)

Table 2 Study design. FIO_2 was set at 0.21 during all measurements

Criteria for eligibility	Criteria for extubation	Criteria for NPPV use	Criteria for reintubation
Intubation > 72 h	$PaO_2 \geq 40$ mm Hg	$PaO_2 < 50$ mm Hg	$PaO_2 < 40$ mm Hg
T-piece trial	$PaCO_2 \leq 55$ mm Hg	$PaCO_2 > 45$ mm Hg	$PaCO_2 > 55$ mm Hg
O_2 cont. > 12 vol. %	pH ≥ 7.32 $V_T \geq 3$ ml/kg RR ≤ 40 beats/min $f/V_T < 190$ NIF ≥ – 20 cmH_2O	pH < 7.35 $V_T < 4$ ml/kg RR > 25 beats/min	pH < 7.32 $V_T < 3$ ml/kg RR > 40 beats/min

Introduction

The risk of complications of invasive mechanical ventilation is related to the duration of ventilatory support [1]. Therefore, discontining invasive mechanical ventilation early is a primary goal in intensive care medicine. A number of studies have been published investigating predictors of weaning outcome [2–4] and successful weaning methods [5–8]. However, the incidence of weaning failure is still high and amounts to approximately 20 % in different studies [5, 7, 8]. A major cause of weaning failure is acute respiratory failure due to respiratory muscle fatigue or increased work of breathing due to decreased pulmonary compliance or increased resistance [3].

Noninvasive positive pressure ventilation (NPPV) is a suitable approach for the treatment of patients with acute respiratory failure [9], particularly those with acute hypercapnic respiratory failure [10–17]. In a recent study, the benefit of NPPV in weaning patients with respiratory failure due to chronic obstructive pulmonary disease (COPD) was demonstrated [18]. The aim of this prospective, interventional study was to investigate the effects of two different modes of noninvasive positive ventilatory support in non-COPD patients with acute respiratory failure after early extubation. We examined the influence of NPPV on pulmonary gas exchange, breathing pattern, intrapulmonary shunt fraction, oxygen consumption, resting energy expenditure, and, finally, weaning success.

Patients and methods

After Ethics Committee approval and written informed consent were obtained, 15 mechanically ventilated patients were included in the study. Demographic data for the study population are given in Table 1.

All patients had to fulfill the following criteria of eligibility (Table 2): mechanical ventilation via an endotracheal tube for a minimum of ≥ 72 h, an oxygen saturation of ≥ 90 % supplemented by max. 6 l O_2/min while breathing spontaneously via a T-tube at ambient air pressure for 5 min, an arterial O_2 content (PaO_2)

≥ 12 volume percent. The criteria for early extubation were measured at the end of the trial at an fractional inspired oxygen of 0.21: $PaO_2 \geq 40$ mm Hg, arterial carbon dioxide ($PaCO_2$) ≤ 55 mm Hg, pH > 7.32, respiratory rate (RR) ≤ 40 breaths per min, tidal volume (V_T) ≥ 3 ml/kg, rapid shallow breathing index (f/V_T) ≤ 190 breaths per min/l, and negative inspiratory force (NIF) ≥ – 20 cmH_2O. All patients were informed about the increased risk of reintubation and instructed in detail about treatment with NPPV. All patients agreed to be extubated. The patients were monitored by means of an arterial and pulmonary artery catheter (PAC) and indirect calorimetry. There were clinical indications for the use of a PAC prior to the study period. All patients were informed about continuing PAC catheterization for study purposes. Nonpulmonary inclusion criteria were as follows: a fully cooperative patient, hemodynamic stability, absence of fever, no facial anomaly to ensure proper fitting of the mask, and no history of claustrophobia. Persistent respiratory insufficiency after extubation was diagnosed when two of the following criteria were present 30 min after extubation: $PaO_2 \leq 50$ mm Hg, $PaCO_2 \geq 45$ mm Hg, pH ≤ 7.35, $V_T \leq 4$ ml/kg, RR ≥ 25 beats/min. Subsequently, the NPPV protocol was instituted. Criteria for reintubation during the study were a $PaO_2 < 40$ mm Hg, $PaCO_2 > 55$ mm Hg, pH < 7.32, $V_T < 3$ ml/kg, RR > 40 beats/min, endotracheal intubation needed for airway protection (coma, seizure disorders), or hemodynamic instability. Exclusion criteria included age < 18 years, use of catecholamines to maintain a systolic blood pressure > 90 mm Hg or a heart rate < 60 beats/min, electrocardiographic instability defined as evidence of ischemia or significant arrhythmias, history of unstable angina or recent (< 3 months) myocardial infarction, additional pharmacological treatment like bronchodilators or steroids. Physiotherapy was withheld during the measurement periods to eliminate any influence due to this physical exercise.

Respirators and masks

Patients received noninvasive mechanical ventilatory support by the same ventilator used during invasive mechanical ventilation before: Servo 300 (Siemens, Stockholm, Sweden); 7200a (Puritan Bennett, Carlsbad, USA); Evita I (Dräger, Lübeck, Germany); Veolar (Hamilton, Rhäzüns, Switzerland) with heated humidifiers (Kendall, Neustadt, Germany; Fisher and Paykel, Auckland, Zew Zealand; Puritan Bennett, Carlsbad, USA; Dräger, Lübeck, Germany). For face mask ventilation, a clear, air-sealed, full face mask (King Systems, Indiana, USA), which was connected via a Y-piece to the respirator, was fitted onto the patient using rubber head straps [9]. Nose masks (Respironics, USA) were held in position by a head cup. Initially, NPPV was applied via the face mask.

Ventilatory support

Patients were treated with two modes of NPPV starting 30 min after extubation with continuous positive air pessure (CPAP) 5 cmH_2O for 30 min followed directly by pressure support ventilation (PSV) 15 cmH_2O with positive end-expiratory pressure (PEEP) 5 cmH_2O for another 30 min. If study values proved beneficial, PSV with PEEP for a minimum of 30 min was administered at least six times per day. The NPPV periods were extended as long as the patients felt comfortable. In the periods off NPPV, patients received supplemental oxygen to achieve an oxygen saturation ≥ 90 % and they were allowed to take enteral fluids and light nutrition (after a fasting period of 6 h after extubation). To minimize the risk of aspiration, the patients were instructed to remove the face mask by themselves in case of severe nausea, and initially the head of the bed was kept elevated at a ≥ 45° angle. Patients were weaned from NPPV by titrating PSV down to zero above PEEP (= CPAP) and by prolonging the periods off NPPV, based on the patient's tolerance and respiratory conditions. NPPV was discontinued when the following breathing values were maintained without any ventilatory support during a 4-h period: RR < 25/min, arterial blood gas analysis: $PaO_2 \geq 55$ mm Hg, $PaCO_2 \leq$ 45 mm Hg, pH > 7.35, fractional inspired oxygen (FIO_2) 0.21. Weaning was considered successful if the patient did not need to be reintubated.

Measurements

The following parameters such as PaO_2, $PaCO_2$, pH, V_T, RR, expired minute ventilation (V_E), f/V_T, Qs/Qt intrapulmonary shunt fraction, VO_2 oxygen consumption, REE resting energy expenditure, and hemodynamic parameters such as heart rate, mean arterial pressure, cardiac index (CI), mean pulmonary arterial pressure, and pulmonary capillary wedge pressure, and blood lactate as a parameter for global tissue oxygenation were measured during spontaneous breathing and during the NPPV protocol (CPAP vs PSV). V_T, RR, and V_E during spontaneous breathing were measured using the Respiradyne II Plus System (self-calibrating spirometer, Sherwood Medical, St. Louis, Mo., USA). During NPPV, V_T, RR, and V_E were recorded continuously by the ventilators. Arterial and mixed venous blood samples were obtained from the arterial catheter (Vygon, Ecouen, France) and the pulmonary artery catheter (Baxter Health Care, CA, USA), respectively, and then analyzed by a blood gas analyzer (ABL 520, Radiometer, Copenhagen, Denmark). The Qs/Qt was calculated by the ABL 520 according to a standard formula [19]. REE and VO_2 were calculated using the metabolic monitor (Deltatrac MBM-100; Datex, Helsinki, Finland) as an indirekt calorimeter. A two-lead electrocardiogram, systemic and pulmonary artery pressures, and arterial oxygen saturation (pulse oximetry) were all recorded continuously (Sirecust 1281; Siemens, Erlangen, Germany).

After extubation all patients were initially breathing spontaneously at ambient air pressure. Oxygen was supplemented to achieve an arterial oxygen saturation ≥ 90 %. After 30 min control measurements (FIO_2 0.21) for SPB and calorimetric analysis (steady state: constant carbon dioxide consumption (VCO_2)/VO_2 for 15–20 min) were taken. Thereafter CPAP was applied for 30 min. Subsequently, PSV with PEEP was administered for the same time interval. CPAP and PSV were applied via the face mask and kept stable (steady state: constant VCO_2/VO_2) for 15–20 min before further measurements were taken. Before all measurements, the FIO_2 was set to 0.21 for 5 min. After the first NPPV episode, a second blood gas analysis was done during spontaneous breathing (SPB^1) as a second control measurement to assess the persistence of respiratory failure without ventilatory support. However, in 3 patients with severe hypoxemia ($PaO_2 < 42$ mm Hg after extubation), the NPPV protocol was changed. These patients were first treated with PSV, followed by CPAP. The data obtained from these 3 patients revealed the same effects as in the other 12 patients who were treated using CPAP first.

Statistical analysis

Differences between spontaneous breathing and the various modes of NPPV were tested using repeated measures analysis of variance and Student-Newman-Keul's tests as post hoc tests. A p value of < 0.05 was considered statistically significant.

Table 3 Effects of different modes of intermittent NPPV (CPAP vs PSV) as compared to spontaneous breathing SPB. After treatment with NPPV blood gas analyses during spontaneous breathing (SPB[1]) were taken again as a second control measurement. FIO_2 was set at 0.21 during all measurements. Values are mean ± SD (*n. d.* not determined)

	SPB	CPAP	PSV	SPB[1]
FIO_2	0.21	0.21	0.21	0.21
PaO_2 (mm Hg)	46 ± 4	57 ± 5*	67 ± 6*#	49 ± 5°#
$PaCO_2$ (mm Hg)	43 ± 7	40 ± 6	37 ± 7*	42 ± 5°
pH	7.41 ± 0.06	7.43 ± 0.05	7.46 ± 0.05*#	7.42 ± 0.04°
V_T (ml/kg)	4 ± 1	5 ± 1*	8 ± 2*#	n. d.
RR (beats/min)	29 ± 6	23 ± 5*	20 ± 5*#	26 ± 6°
V_E (l/min)	7.8 ± 2.1	8.1 ± 1.9	9.7 ± 0.9*	n. d.
f/V_T (min^{-1}/l)	123 ± 37	56 ± 17*	37 ± 12*#	n. d.
Qs/Qt (%)	27 ± 3	20 ± 4*	15 ± 3*#	n. d.
VO_2 (ml/min)	241 ± 15	204 ± 9*	187 ± 13*#	n. d.
REE (kcal/day)	1658 ± 220	1454 ± 204*	1332 ± 234*#	n. d.

* $p < 0.05$ compared with SPB; # $p < 0.05$ compared with CPAP; ° $p < 0.05$ compared with PSV

Table 4 Hemodynamic variables measured during spontaneous breathing and NPPV. Values are mean ± SD (*HR* heart rate, *MAP* mean arterial pressure, *MPAP* mean pulmonary artery pressure, *PCWP* pulmonary capillary wedge pressure, *CI* cardiac index, PvO_2 mixed venous oxygen tension)

	SPB	CPAP	PSV	Significance
HR (min^{-1})	101 ± 12	98 ± 8	95 ± 8	NS
MAP (mm Hg)	85 ± 13	83 ± 10	84 ± 13	NS
MPAP (mm Hg)	23 ± 4	22 ± 3	21 ± 2	NS
PCWP (mm Hg)	15 ± 3	14 ± 5	15 ± 5	NS
CI (l/min per m^2)	3.1 ± 0.5	2.8 ± 0.4	2.9 ± 0.6	NS
Lactate (mmol/l)	1.2 ± 0.3	0.9 ± 0.5	1.1 ± 0.3	NS
PvO_2 (mm Hg)	35 ± 3	36 ± 3	36 ± 3	NS

Results

Fifteen patients were included in the study (7 females). They had required invasive mechanical ventilation via an endotracheal tube for a median of 8 days (range 3–60 days). Four patients were on Servo 300, 4 patients on a Puritan Bennett 7200a, 4 patients on Evita I, and 3 other patients on Veolar ventilators both during invasive mechanical ventilation and during the NPPV study period. Changes in the respiratory parameters during the different modes of NPPV are given in Table 3.

The median duration of NPPV was 2 days (range 1–20 days) with a mean duration of 8.5 ± 1.7 h. Four patients were weaned from NPPV within 24 h. In 9 patients, pressure support was reduced from 15 to 10 cmH_2O within the first 24 h. One patient who required NPPV for 20 days had received a lung transplant because of cystic fibrosis with cachexia. This patient was finally weaned successfully. None of the patients rejected NPPV. No side effects due to NPPV occurred. Depending on the patient's condition (sufficient oral muscle tension to keep the mouth closed), nose mask ventilation was preferred in 6 patients. No difference was noted in the effects of NPPV using either the face or the nose mask.

Hemodynamic parameters showed no significant changes during NPPV when compared with spontaneous breathing (Table 4). Two patients had to be reintubated within the first 48 h (rate of successful weaning 87 %). One patient developed a drug-related encephalopathy resulting in impairment of vigilance and loss of protection reflexes. The other developed acute rejection of the transplanted lung with systemic inflammatory response syndrome and recurrent acute respiratory failure. This patient was the only one in the study group who died (hospital mortality).

Discussion

The results of this study demonstrate that NPPV is feasible to treat acute respiratory failure after early extubation. NPPV improves respiratory parameters such as PaO_2, $PaCO_2$, pH, RR, V_T, f/V_T, Qs/Qt, VO_2, and REE with increasing ventilatory support (CPAP vs PSV; Table 3) in non-COPD patients. Katz and Marks [20] showed that CPAP enhances the functional residual capacity, resulting in improvements of lung mechanics and pulmonary gas exchange and in a reduction of the work of breathing. PSV augments the transpulmonary

pressures [13], leading to an increased V_T and a decreased RR. The reduction in work of breathing, the correction of respiratory acidosis, and the prevention of hypoxemia together result in a recovery and reconditioning of respiratory muscle function [21].

NPPV has been used successfully as an alternative to endotracheal intubation in patients with acute hypercapnic [15, 16, 22–25] and hypoxemic [9] respiratory failure. Nava et al. [18] have demonstrated in a multicenter randomized trial a long-term benefit of NPPV compared to persistent mechanical ventilation in weaning patients with respiratory failure due to chronic respiratory disease. Hilbert et al. [26] concluded that NPPV may be used in COPD patients with hypercapnic respiratory insufficiency after extubation. These authors clearly showed in their prospective interventional study beneficial effects of NPPV on pulmonary gas exchange, breathing pattern, Qs/Qt, VO_2, and REE in non-COPD patients after early discontinuation of invasive mechanical ventilation despite continuing acute respiratory failure. All parameters improved significantly during CPAP compared to spontaneous breathing with the exception of $PaCO_2$ and pH. Again, the values for PaO_2, V_T, f/V_T, VO_2, REE, Qs/Qt also significantly improved using PSV compared with CPAP. These findings are in accordance with the results of Appendini et al. [27], who demonstrated that the combination of CPAP and PSV provided more beneficial effects than CPAP alone in COPD patients. According to the study of Putensen et al. [28], there was no difference in the effectiveness of NPPV using either face or nose mask. However, patients seemed more comfortable using nasal mask ventilation. As observed in other studies [10, 16], hemodynamic variables (Table 3) did not change significantly during NPPV. Diaz et al. [29] observed a fall in cardiac output during NPPV with no impact on mixed venous oxygen tension (PvO_2). In our study, CI and PvO_2 remained unchanged during NPPV, whereas Qs/Qt and VO_2 declined.

The criteria for early extubation applied in this study ($V_T \geq 3$ ml/kg, RR ≤ 40 breaths/min, $f/V_T \leq 190\ min^{-1}/l$, and NIF $\geq -20\ cmH_2O$) were much more liberal than those proposed by Yang and Tobin [2] ($V_T \geq 4$ ml/kg, RR ≤ 38 breaths/min, $f/V_T \leq 105$), Krieger et al. [4] ($f/V_T \leq 130$), Esteban et al. [5] ($V_T \geq 5$ ml/kg, RR ≤ 35 breaths/min), and Brochard et al. [8] (RR ≥ 35 breaths/min, NIF $\geq -25\ cmH_2O$). Consequently, it could be hypothesized that without intermittent NPPV in the majority of our patients extubation would have been unsuccessful. Shikora and colleagues [30] showed that the oxygen cost of breathing (OCOB) – derived from the difference in measured VO_2 during total ventilatory support and spontaneous breathing at CPAP – proved to be a reliable predictor of both successful extubation and weaning failure. They found that patients are unlikely to maintain spontaneous ventilation if the OCOB is elevated more than 15% above total-body VO_2. In our study, NPPV reduced oxygen consumption by about 22% during PSV and by approximately 15% during CPAP compared to spontaneous breathing.

It has been suggested that NPPV decreases pulmonary ventilation-perfusion ratio [14]. In our study, the implementation of increased transpulmonary pressures by NPPV diminished intrapulmonary shunt and improved pulmonary gas exchange. We suppose that NPPV was able to recruit nonventilated lung units, thereby reducing Qs/Qt and PvO_2.

The study protocol was limited by some limitations. First, we evaluated the respiratory effects of NPPV (CPAP vs PSV) compared with spontaneous breathing using each patient as his/her own control (SPB and SPB^1). A control group was not recruited because we expected that the patients under study would not be able to breathe without any respiratory support for a longer period of time. In addition, we expected a high reintubation rate in a control group treated only with oxygen. Second, the order of CPAP followed by PSV was not randomized. In 3 patients we started with noninvasive PSV followed by CPAP. However, the data from these 3 patients revealed similar effects compared to the results obtained from patients starting with CPAP. Third, the number of transplant recipients in our study group is high. One of our main efforts in this patient population was to discontinue mechanical ventilation as early as possible to reduce the risk of infection.

To obtain reliable data when comparing different modes of ventilation (spontaneous breathing, CPAP, PSV) the FIO_2 was set at 0.21. This design was used, since spontaneous breathing with an oxygen face mask results in unpredictable variations in the FIO_2 [31]. Again, any change in the ventilatory pattern will also vary the FIO_2 [32]. We presume that we did not harm the patients because their blood lactate levels and cardiac output (Table 4) remained unchanged during study. Eldridge [33] and Lundt et al. [34] reported no signs of tiusse hypoxia using lactate as a marker of tissue hypoxia in patients with severe hypoxemia ($PaO_2 < 40$ mm Hg) as long as the cardiac output remained within the normal range.

We conclude that intermittent NPPV (CPAP and PSV) is a feasible therapeutic option in non-COPD patients with acute respiratory failure after extubation. NPPV improves the breathing pattern, decreases Qs/Qt, and reduces work of breathing. From these results one could hypothesize that intermittent NPPV may allow earlier extubation and may reduce weaning failure in patients after prolonged mechanical ventilation. Controlled clinical trials to test this hypothesis are warranted.

References

1. Fagon JY, Chastre J, Domart Y, Trouillet J-L, Pierre J, Darne CH, Gibert C (1989) Nosocomial pneumonia in patients receiving continuous mechanical ventilation: prospective analysis of 52 episodes with the use of a protected specimen brush and quantitative culture techniques. Am Rev Respir Dis 139: 877–884
2. Yang KL, Tobin MJ (1991) A prospective study of indexes predicting the outcome of trials of weaning from mechanical ventilation. N Engl J Med 324: 1445–1550
3. Lee KH, Hui KP, Chan TB, Tan WC, Lim TK (1994) Rapid shallow breathing (frequency-tidal volume ratio) did not predict extubation outcome. Chest 105: 540–543
4. Krieger BP, Isber J, Breitenbucher A, Throop G, Ershowsky P (1997) Serial measurements of rapid-shallow-breathing index as a predictor of weaning outcome in elderly medical patients. Chest 112: 1029–1034
5. Esteban A, Frutos F, Tobin MJ, Alia I, Solsona JF, Valverdu I, Fernandez R, de la Cal MA, Benito S, Tomas R, Carriedo D, Macias S, Blanco J (1995) A comparison of four methods of weaning patients from mechanical ventilation. N Engl J Med 332: 345–350
6. Esteban A, Alia I, Ibanez J, Bonito S, Tobin MJ (1994) Modes of mechanical ventilation and weaning: a national survey of Spanish hospitals. Chest 106: 1188–1193
7. Esteban A, Alia I, Gordo F, Fernandez R, Solsona JF, Vallverdu I, Macias S, Allegue JM, Blanco J, Carriedo D, Leon M, de la Cal M, Taboada F, Gonzalez de Velasco J, Palazon E, Carrizosa F, Tomas R, Suarez J, Goldwasser RS (1997) Extubation outcome after spontaneous breathing trials with T-tube or pressure support ventilation. Am J Respir Crit Care Med 156: 459–465
8. Brochard L, Rauss A, Benito S, Conti G, Mancebo J, Rekik N, Gasparetto A, Lemaire F (1994) Comparison of three methods of gradual withdrawal from ventilatory support during weaning from mechanical ventilation. Am J Respir Crit Care Med 150: 896–903
9. Antonelli M, Conti G, Rocco M, Bufi M, Alberto de Blasi R, Vivino G, Gasparetto A, Meduri GU (1998) A comparison of noninvasive positive-pressure ventilation and conventional mechanical ventilation in patients with acute respiratory failure. N Engl J Med 339: 429–435
10. Meduri GU, Abou-Shala N, Fox RC, Jones CB, Leeper KV, Wunderink RG (1991) Noninvasvie face mask mechanical ventilation in patients with acute hypercapnic respiratory failure. Chest 100: 445–454
11. Meduri GU, Fox RC, Abou-Shala N, Leeper KV, Wunderink RG (1994) Noninvasive mechanical ventilation via face mask in patients with acute respiratory failure who refused endotracheal intubation. Crit Care Med 22: 1584–1590
12. Meduri GU, Turner RE, Abou-Shala N, Wunderink R, Tolley E (1996) Noninvasive positive pressure ventilation via face mask. Cehst 109: 179–193
13. Abou-Shala N, Meduri GU (1996) Noninvasive mechanical ventilation in patients with acute respiratory failure. Crit Care Med 25: 705–715
14. Meyer TJ, Hill NS (1994) Noninvasive positive pressure ventilation to treat respiratory failure. Ann Intern Med 120: 760–770
15. Brochard L, Mancebo J, Wysocki M, Lofaso F, Conti G, Rauss A, Simonneau G, Benito S, Gasparetto A, Lemaire F, Isabey D, Harf A (1995) Noninvasive ventilation for acute exacerbation of chronic obstructive pulmonary disease. N Engl J Med 333: 817–822
16. Kramer N, Meyer TH, Meharg J, Cece RD, Hill NS (1995) Randomized, prospective trial of noninvasive positive pressure ventilation in acute respiratory failure. Am J Respir Crit Care Med 151: 1799–1806
17. Wysocki M, Tric L, Wolff MA, Millet H, Herman B (1995) Noninvasive pressure support ventilation in patients with acute respiratory failure. A randomized comparison with conventional therapy. Chest 107: 761–768
18. Nava S, Ambrosino N, Clini E, Prato M, Orlando G, Vitacca M, Brigada P, Rubini F (1998) Noninvasive mechanical ventilation in the weaning of patients with respiratory failure due to chronic obstructive pulmonary disease. Ann Intern Med 128: 721–728
19. Ogawa S, Kusonoki M, Shirai J, Takeda K, Takezawa J, Tenaka N, Matsumoto M, Kamada T (1989) Prediction of arterial oxygen partial pressure from intrapulmonary venous admixture. Crit Care Med 17: 1191
20. Katz JA, Marks JD (1985) Inspiratory work with and without continuous positive airway pressure in patients with acute respiratory failure. Anesthesiology 63: 598–607
21. Brochard L, Isaby D (1994) Noninvasive positive pressure ventilation for acute respiratory failure. In: Vincent JL (ed) Yearbook of intensive care and emergency medicine. Springer, Berlin Heidelberg New York, pp 554-558
22. Bott J, Caroll MP, Conway JH, Keilty SEJ, Ward EM, Brown AM, Paul EA, Elliot MW, Godfrey RC, Wedzicha JA, Moxham J (1993) Randomised controlled trial of nasal ventilation in acute ventilatory failure due to chronic obstructive airway disease. Lancet 341: 1555–1557
23. Pennock BE, Kaplan PD, Carlin BW, Sabangan JS, Magovern JS (1991) Pressure support ventilation with a simplified ventilatory support system administered with a nasal mask in patients with respiratory failure. Chest 100: 1371–1376
24. Wysocki M, Tric L, Wolff MA, Gertner J, Millet H, Herman B (1993) Noninvasive pressure support ventilation in patients with acute respiratory failure. Chest 103: 907–913
25. Pennock BE, Crawshaw L, Kaplan PD (1994) Noninvasive nasal mask ventilation for acute respiratory failure. Institution of a new therapeutic technology for routine use. Chest 105: 441–444
26. Hilbert G, Gruson D, Portel L, Gbikpi-Benissan G, Cardinaud JP (1998) Noninvasive pressure support ventilation in COPD patients with postextubation hypercapnic respiratory insufficiency. Eur Respir J 11: 1349–1353
27. Appendini L, Patessio A, Zanaboni S, Carone M, Gukov B, Donner CF, Rossi A (1994) Physiologic effects of positive end-exspiratory pressure and mask pressure support during exacerbation of chronic obstructive pulmonary disease. Am J Respir Crit Care Med 149: 1069–1076
28. Putensen C, Hörmann C, Baum M, Lingnau W (1993) Comparison of mask and nasal continuous positive airway pressure after extubation and mechanical ventilation. Crit Care Med 21: 357–362
29. Diaz O, Iglesia R, Ferrer M, Zavala E, Santos C, Wagner PD, Roca J, Rodriguez-Roisin R (1997) Effects of noninvasive ventilation on pulmonary gas exchange and hemodynamics during acute hyercapnic exacerbations of chronic obstructive pulmonary disease. Am J Respir Crit Care Med 156: 1840–1845

30. Shikora SA, Benotti PN, Johannigmann JA (1994) The oxygen cost of breathing may predict weaning from mechanical ventilation better than the respiratory rate to tidal volume ratio. Arch Surg 129: 269–274
31. Shapiro BA, Kacmarek RM, Cane RD (1991) Clinical application of respiratory care, 4th edn. Mosby, St. Louis, pp 123–134
32. O'Connor BS, Vender JS (1995) Oxygen therapy. Crit Care Clin 11: 67–78
33. Eldridge FE (1966) Blood lactate and pyruvate in pulmonary insufficiency. N Engl J Med 274: 878–883
34. Lundt T, Koller M, Kofstad J (1984) Severe hypoxemia without evidence of tissue hypoxia in adult respiratory distress syndrome. Crit Care Med 12: 75–76