

## Noninvasive positive pressure ventilation in patients with perioperative negative pressure pulmonary edema

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**Abstract** Negative pressure pulmonary edema (NPPE) is a noncardiogenic pathological process that is treated with invasive ventilation via a tracheal tube. To investigate the feasibility and safety of noninvasive positive pressure ventilation (NPPV) as an alternative treatment for NPPE, we retrospectively reviewed charts of 15 perioperative NPPE patients. Eight patients were treated by NPPV and 7 were treated by invasive ventilation. Patient characteristics, duration of NPPV, duration of intensive care unit (ICU) stay, and maximum airway pressure were investigated for the NPPV-treated patients. All patients treated by NPPV had a patent airway after complete relief of the airway obstruction and recovered from NPPE symptoms within one postoperative day. Arterial blood gas analysis showed a significant improvement in the PaO<sub>2</sub>/FiO<sub>2</sub> ratio from 132 ± 30 mmHg in the operating room to 282 ± 77 mmHg at discontinuation of NPPV. Serious complications, such as ventilator-associated pneumonia or aspiration pneumonia, did not occur, and intubation was not required for any patient. Favorable outcomes in these cases suggest that NPPV could be a feasible and safe alternative for treating NPPE if the patency of the airway is restored.

**Keywords** Noninvasive positive pressure ventilation · Negative pressure pulmonary edema · Pulmonary edema · Perioperative airway obstruction

### Introduction

Negative pressure pulmonary edema (NPPE) is an uncommon complication defined as a noncardiogenic pathological process in which transudation of fluid into the pulmonary interstitium occurs in response to the generation of markedly negative intrathoracic pressure [1–3]. The general symptoms and clinical findings are basically similar to those of pulmonary edema caused by other etiologies but are reported to remain for a shorter period [2, 4–7]. The first-line treatment for severe cases of NPPE that require active airway intervention is the administration of positive end-expiratory pressure (PEEP) and mechanical ventilation via a tracheal tube [3, 5].

Noninvasive positive pressure ventilation (NPPV) is a standard treatment for acute cardiogenic pulmonary edema, and the improvement in the mortality rate is evident [8, 9]. It is also reported that, with selected patients, NPPV will benefit hypoxemic respiratory failure [10, 11]. However, the efficacy of NPPV for NPPE, another type of pulmonary edema, is not well understood, and only a few case studies have examined the eligibility of NPPV for perioperative NPPE [7]. To receive the full benefit of NPPV, we routinely apply this treatment as often as possible. As a result, we have experienced several cases of NPPE during the perioperative period that were successfully treated with NPPV. Thus, we retrospectively analyzed our cases and assessed the effectiveness and safeness of NPPV against NPPE patients and also clarified its limitations.

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## Methods

We retrospectively reviewed the cases of 15 patients who presented clinical symptoms and met the diagnosis of NPPE in the perioperative period between May 2004 and July 2008. The diagnosis of NPPE was based on roentgenographic evidence and arterial blood gas analysis, in addition to the physical findings of pulmonary congestion and infiltration with a concomitant intrathoracic negative pressure episode. The absence of known cardiopulmonary diseases, drug hypersensitivity, aspiration, and fluid overload were also assessed, and patients with a known pathology that could lead to pulmonary edema were excluded.

The criteria for NPPV application we followed are generally consistent with previous literature that refers to the acute applications and clinical guidelines for NPPV [12]. On a daily basis, we applied NPPV as often as possible to convey the full benefit for patients with respiratory insufficiency. The age, sex, airway management during the operation, NPPV ventilation mode and maximum airway pressure administered, duration of NPPV, and the duration of the intensive care unit (ICU) stay were determined for each patient. Airway complications during NPPV treatment were also reviewed. Data from the arterial blood gas analysis were examined at four time points: at discharge from the operating room, immediately after starting NPPV in the ICU, at the time of discontinuation of NPPV, and at discharge from the ICU. We also reviewed charts of NPPE patients who were not treated by NPPV but by invasive ventilation, e.g., tracheal intubation or tracheotomy.

A BiPAP Vision (Respironics, Murrysville, PA, USA) device was used for the administration of NPPV. For the purpose of this study, continuous positive airway pressure (CPAP) and bilevel positive airway pressure (bilevel-PAP) ventilation via a facemask were deemed part of NPPV.

Repeated-measures analysis of variance and Bonferroni's multiple-comparison tests were performed to distinguish differences over time, with  $P < 0.01$  considered to indicate a significant difference. All statistical analyses were carried out with Dr. SPSS II (SPSS, Chicago, IL, USA). Data are expressed as the mean  $\pm$  standard deviation unless otherwise indicated.

## Results

The overall prevalence of NPPE throughout the 50-month study period was 0.056% (15 of 26,846). Eight patients were treated by NPPV and 7 by invasive ventilation. Patient characteristics, airway management during operation, the negative pressure episode and the NPPE type, NPPV settings and duration at the ICU, and the duration of

the ICU stay for all patients examined are shown in Table 1. The eight patients treated by NPPV were able to restore their airway by either head tilt, chin lift, or jaw thrust until they could self-protect their airway after complete emergence from anesthesia; they were also capable of manual-assist ventilation by face mask. The seven patients treated by invasive ventilation had either a life-threatening laryngospasm requiring immediate tracheal intubation (patients 9, 12, 13), instability of the upper airway due to delayed emergence from anesthesia (patients 10, 11), or a tracheal suture by relief surgery of tracheal stenosis (patients 14, 15). With close review of the charts, patients 10 and 11 had impaired consciousness and could not protect their own airway, yet it was difficult to maintain the airway by manual procedure, and they had a strong respiratory drive to produce negative intrathoracic pressure. Patients 14 and 15 were treated by tracheotomy to isolate the surgical site from NPPV airway pressure or mechanical stress by tracheal intubation. Thirteen patients met the criteria for type 1 NPPE (upper airway obstruction) and 2 met the criteria for type 2 NPPE (sudden relief of chronic auto-PEEP). For the NPPV-treated patients, arterial blood gas analyses at the onset of NPPE are also shown in Table 1.

The  $\text{PaO}_2/\text{FiO}_2$  ratio and  $\text{SpO}_2$  improved in all patients promptly after the application of NPPV, and the improvements in the  $\text{PaO}_2/\text{FiO}_2$  ratio at the three later time points were statistically significant ( $P < 0.01$ ) (Table 2). The pH of the three acidotic patients and  $\text{PaCO}_2$  in the five hypercapnic patients also improved promptly, but the improvement of  $\text{PaCO}_2$  did not show a statistical significance ( $P = 0.047$ ) (Table 2). All NPPV-treated patients were discharged from the ICU within one postoperative day ( $21.4 \pm 3.0$  h), and none required intubation after NPPV treatment. All patients were sufficiently conscious to protect their own airway throughout the treatment period, and there were no significant complications such as ventilator-associated pneumonia or aspiration pneumonia.

## Discussion

Our study indicated the feasibility, efficacy, and safety of NPPV for the treatment of selected perioperative NPPE patients by promptly improving respiratory function without serious complications. We also emphasize here that only an NPPE patient with clear consciousness and patent airway after complete relief of the airway obstruction is a candidate for NPPV. Previous studies have suggested, not for NPPE but in general, that NPPV should be administered to limited patients [10, 12]. Because of the nature of postoperative NPPE, which is most often accompanied by insecurity of the airway and impaired consciousness caused

**Table 1** Patient characteristics

Patient characteristics and NPPE details				NPPV setting at the ICU		Duration of ICU stay		ABG before NPPV at the operating room					
NPPV patients	Age	Sex	Airway management during surgery	Negative pressure episode	NPPE type	NPPV mode	Maximum NPPV pressure (cmH <sub>2</sub> O)	Duration of NPPV	Duration of ICU stay	PaO <sub>2</sub> /FiO <sub>2</sub> (mmHg)	PaCO <sub>2</sub> (mmHg)	pH	SpO <sub>2</sub> (%)
Patients treated with NPPV													
1	72	Female	LMA	Missfit of LMA during surgery	Type 1	CPAP	6	17 h 42 min	23 h 55 min	93	36	7.48	81
2	73	Male	LMA	Missfit of LMA during surgery	Type 1	CPAP	4	1 h 35 min	25 h 32 min	146	47	7.37	84
3	55	Female	LMA	Missfit of LMA during surgery	Type 1	Bilevel-PAP	IPAP 12 EPAP 4	16 h 03 min	20 h 23 min	92	40	7.48	83
4	27	Male	LMA	Missfit of LMA during surgery	Type 1	CPAP	12	2 h 50 min	15 h 32 min	118	45	7.38	89
5	69	Female	Tracheal intubation	Obstruction during difficult airway induction	Type 1	CPAP	6	21 h 10 min	21 h 45 min	149	50	7.35	92
6	58	Male	Tracheal intubation	Obstruction during difficult airway induction	Type 1	CPAP	8	17 h 40 min	23 h 15 min	179	69	7.23	98
7	40	Male	Tracheal intubation	Airway obstruction after extubation	Type 1	CPAP	6	30 h 15 min	20 h 15 min	130	54	7.32	88
8	63	Male	Tracheal intubation	Airway obstruction after extubation	Type 1	CPAP	6	17 h 40 min	20 h 50 min	151	44	7.41	93
							6.0 ± 1.3 (excluding patient 3)	14.4 ± 7.7	21.4 ± 3.0	132 ± 30	48 ± 10	7.38 ± 0.08	89 ± 6
Patient characteristics and NPPE details													
Airway management at the ICU				NPPE type		IV technique at the ICU		Duration of ICU stay					
IV patients	Age	Sex	Airway management during surgery	Negative pressure episode	NPPE type	IV technique at the ICU	Duration of IV	Duration of ICU stay	Duration of ICU stay	Duration of ICU stay	Duration of ICU stay	Duration of ICU stay	Duration of ICU stay
Patients treated with IV													
9	77	Female	Tracheal intubation	Laryngospasm after extubation	Type 1	Tracheal intubation	91 h 20 min	113 h 25 min					
10	58	Male	Tracheal intubation	Airway obstruction after extubation	Type 1	Tracheal intubation	21 h 55 min	64 h 35 min					
11	71	Male	LMA	Airway obstruction after LMA removal	Type 1	Tracheal intubation	21 h 30 min	25 h 00 min					
12	70	Male	Tracheal intubation	Laryngospasm after extubation	Type 1	Tracheal intubation	32 h 50 min	57 h 30 min					
13	70	Female	Tracheal intubation	Laryngospasm after extubation	Type 1	Tracheal intubation	32 h 50 min	62 h 40 min					
14	44	Male	Tracheal intubation	Relief of chronic airway stenosis	Type 2	Tracheotomy	77 h 00 min	118 h 30 min					
15	48	Female	Tracheal intubation	Relief of chronic airway stenosis	Type 2	Tracheotomy	17 h 35 min	20 h 00 min					
							42.1 ± 29.6	66.0 ± 38.5					

The upper table shows patient characteristics, NPPE details, NPPV setting at the ICU, duration of the ICU stay, and the ABG at the onset of NPPV for patients treated with NPPV; the lower table shows patient characteristics, NPPE details, airway management at the ICU, and the duration of the ICU stay for patients treated with invasive ventilation

Average data are shown as mean ± standard deviation (SD)

NPPV noninvasive positive pressure ventilation, IV invasive ventilation, NPPE negative pressure pulmonary edema, CPAP continuous positive airway pressure, ICU intensive care unit, ABG arterial blood gas analysis, LMA laryngeal mask airway, Bilevel-PAP bilevel positive airway pressure, IPAP inspiratory positive airway pressure, EPAP expiratory positive airway pressure

**Table 2** Comparison of arterial blood gas data at various time points in the ICU with data in the operating room

	Operating room	Administration of NPPV	Discontinuation of NPPV	Discharge from ICU
pH	7.38 ± 0.08	7.43 ± 0.04*	7.43 ± 0.03*	7.44 ± 0.03*
PaO <sub>2</sub> /FiO <sub>2</sub> (mmHg)	132 ± 30	194 ± 49*	282 ± 77*	230 ± 44*
PaCO <sub>2</sub> (mmHg)	48 ± 10	41 ± 5	41 ± 5	40 ± 4
SpO <sub>2</sub> (%)	89 ± 6	98 ± 1*	98 ± 1*	97 ± 2*

NPPV noninvasive positive pressure ventilation, ICU intensive care unit, ANOVA analysis of variance

\*  $P < 0.01$  compared with data in the operating room; repeated-measures ANOVA with Bonferroni's multiple-comparison test

by remaining anesthetic agents, we believe the attachment of NPPV requires more prudent decisions than for general use. Again reviewing our cases, the anesthesiologists in charge for the NPPV treated patients required at least 1 h at the operation room to decide the treatment course while assisting the airway with manual ventilation, waiting for complete patency of the airway and complete emergence from anesthesia. From our clinical experience, we strongly recommend that one should not abruptly select NPPV without cautious observation and should at least wait until the patient can sufficiently speak and cooperate to the attachment of NPPV. In addition, although there was no such case in our study, we suggest converting from NPPV to invasive ventilation if the gas exchange does not immediately improve after attachment.

The perioperative period is assumed to be the most likely time point for development of NPPE, and the estimated rate of occurrence in previous reports is approximately 0.1% [13, 14], whereas the overall prevalence of NPPE was 0.056% in our study. Compared with the small number of clinical cases reported in the literature (fewer than 200 cases in the past 38 years) [15], the estimated frequency is apparently high, suggesting that NPPE might be underdiagnosed during the perioperative period. Both types of NPPE are potentially life threatening [5, 6], and early recognition and treatment are important for a favorable outcome. In the literature, 66.5–85% of cases of NPPE require tracheal intubation to ensure airway patency and to administer mechanical ventilation [3, 15], and at most 20% of NPPE patients were treated by NPPV [13]. In our study, 53.3% of patients were treated successfully by NPPV. Therefore, together with the underdiagnosed patients, we postulate that a larger proportion of NPPE patients could be treated by NPPV than is described in the literature.

Seven of the eight NPPV-treated patients in our study showed improved gas exchange with CPAP, perhaps because they had sufficiently strong respiratory muscles not only to produce NPPE but also to permit sufficient respiration. In the present study, the maximum NPPV pressure was  $6.0 \pm 1.3$  cmH<sub>2</sub>O, suggesting that the NPPV setting for NPPE need not to be strongly assisted.

In conclusion, NPPE is an emergency disease in which the onset is rapid and usually unexpected. Nevertheless,

once one encounters such a disease, the first priority is without doubt to open the patients' airway immediately. However, for limited patients whose airway is secured, it seems feasible to consider NPPV as a treatment option. We have shown eight perioperative NPPE patients who were efficiently treated using NPPV as an alternative to invasive positive pressure ventilation without serious complications. With such a small study size, however, it is not appropriate to jump to conclusions. Further investigations must be made to confirm the benefit, safety, and limits of NPPV treatment. It is also important for anesthesiologists to understand, avoid, and prepare for NPPE.

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