ORIGINAL ARTICLE

Noninvasive positive pressure ventilation for the treatment of acute respiratory distress syndrome following esophagectomy for esophageal cancer: a clinical comparative study

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ABSTRACT

Objective: To evaluate the therapeutic efficacy of noninvasive positive pressure ventilation (NPPV) in the treatment of acute respiratory distress syndrome (ARDS) following esophagectomy for esophageal cancer.

Methods: In this retrospective evaluation, we included 64 patients with ARDS following esophagectomy for esophageal cancer between January 2009 and December 2011. The primary evaluations were 28-day fatality and actual fatality. The secondary evaluations were sex, age, onset time, pH value, PaO_2/FiO_2, sequential organ failure assessment (SOFA) score, acute physiology and chronic health evaluation (APACHE-II) score, and presence or absence after surgery of major surgery-related complications such as cardiac arrest, anastomotic fistula, and acute renal dysfunction.

Results: NPPV applied as the first-line intervention for ARDS following esophagectomy for esophageal cancer avoided intubation in 30 patients (30/64, 48.4%). There were no significant differences in gender, age, PaO_2/FiO_2, SOFA score, or APACHE-II score between the NPPV group and the patients who required invasive positive pressure ventilation (IPPV group) ($P>0.05$) at the time of onset, while differences in the PaO_2/FiO_2 ($P<0.05$) after 24 h of NPPV and presence of major surgery-related complications were highly significant ($P<0.01$).

Conclusions: NPPV may be an effective option for the treatment of ARDS/acute lung injury (ALI) following esophagectomy for esophageal cancer. However, conversion to invasive mechanical ventilation should be considered in patients with severe postoperative complications such as acute renal dysfunction and cardiac arrest and in those with PaO_2/FiO_2 <180 after 2 h of NPPV.

KEYWORDS Noninvasive positive pressure ventilation (NPPV); esophagectomy; acute respiratory distress syndrome (ARDS)

J Thorac Dis 2013;5(6):777-782. doi: 10.3978/j.issn.2072-1439.2013.09.09

Introduction

Acute respiratory distress syndrome (ARDS) is a clinical complex mainly characterized by alveolar capillary injury and arising from various extra- and intra-pulmonary contributing factors (1-7). It is a severe stage or type of acute lung injury (ALI), clinically presenting as increased respiratory rate and respiratory distress, progressive hypoxemia, and diffuse infiltrations on chest X-ray. Thoracic surgery-related lung injury is likely to be associated with the occurrence of ARDS/ALS (8). The treatment of ARDS is a clinical challenge in thoracic surgery (9-16), and in patients with difficult expectoration, invasive mechanical ventilation requiring endotracheal intubation or tracheostomy is often necessary. However, noninvasive positive pressure ventilation (NPPV) can be an effective technique to improve gas exchange and avoid endotracheal intubation in selected patients with acute respiratory failure (ARF) due to ARDS (17-19). Although NPPV has been used successfully in the treatment of various forms of hypoxemic ARF (20), it efficacy as a treatment for ARDS and ALI remains controversial (21,22). In a meta-analysis of the use of NPPV in the treatment of ARDS/ALI from 1995 through 2009, Agarwal and his colleagues (23)

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Submitted Sep 09, 2013. Accepted for publication Sep 11, 2013.
Available at www.jthoracdis.com

ISSN: 2072-1439

found that NPPV was successful in fewer than 50% of cases. Therefore, they suggested that noninvasive ventilation (NIV) for the treatment of ARDS/ALI should be applied prudently. Nava and colleagues (24) posited that NIV should not be considered in patients with PaO_2/FiO_2 <200, except in those who are hemodynamically stable, while Antonelli M *et al.* (25) argued that NPPV should be recommended as a first-line treatment strategy because it prevented 54% of endotracheal intubations in professional centers. Thus far, there have been only few reports on the use of NPPV in patients following esophagectomy.

The present study is a retrospective analysis to determine the efficacy of NPPV in the treatment of ARDS/ALI following esophagectomy for esophageal cancer. In addition, we aimed to investigate factors related to failure of NPPV in an attempt to further define indications for NPPV in the treatment of ARDS/ALI following esophagectomy.

Methods

Patient selection

After a retrospective review of records of 1,638 patients who received surgical treatment for esophageal or cardial cancer in our hospital between January 2009 and December 2011, we found 64 who had developed ARDS/ALS and remained in the surgical ICU, and these were included in this study. The patients were classified into two groups according to the modality of mechanical ventilation: those treated with NPPV (NPPV group) and those requiring invasive positive pressure ventilation (IPPV group). Treatment of all patients followed the clinical flow chart shown in Figure 1, and the general data of these patients are shown in Table 1.

Treatments and outcome measures

Definition of ARDS/ALI: the diagnoses for all patients were based on the revised diagnostic criteria of North American and European Consensus Conference (25-27), including (I) acute onset; (II) PaO_2/FiO_2 ≤200 mmHg, regardless of PEEP; (III) posteroanterior chest X-ray showing patchy shadows in both lungs; and (IV) presence of hydrostatic pulmonary edema or exclusion of hydrostatic pulmonary edema due to left heart failure. The diagnosis of ALI was confirmed when PaO_2/FiO_2 was ≤300 mmHg in addition to the above criteria.

A cluster treatment scheme using NPPV was applied as the first treatment of choice in 48 patients with ARDS/ALI following esophagectomy. Initial exclusion criteria were hemodynamic or EKG instability, active bleeding, coma or other neurological disturbances, and need for urgent endotracheal intubation to manage secretions or protect the airway. NPPV was converted to IPPV via endotracheal intubation or tracheostomy in 16 patients because of intolerance of NPPV due to pain, discomfort, or claustrophobia; failure to maintain a PaO_2 >65 mmHg with FiO_2 ≤0.6 and persistent dyspnea, tachypnea, and activation of accessory respiratory muscles; hemodynamic instability; and/or need for urgent endotracheal intubation to manage secretions or protect the airways. The ventilator was a PB840 (Tyco, American).

The primary outcome variables were the length of ICU stay, 28-day survival in the ICU and in hospital admission. Secondary endpoints included the number of patients eligible for NPPV, requirement for endotracheal intubation and mechanical ventilation at any time, and risk factors associated with failure of NPPV.

Statistical analysis

Statistical analysis was performed using SPSS 13.0. In single factor analysis, measurement data were tested by *t* test using two independent samples, and enumeration data were tested by chi-square test. P-value of less than 0.05 was considered statistically significant.

Results

We included 64 patients (59 men and 5 women; age range, 49-83 years; mean age, 61.1±7.2 years) with ARDS/ALI following esophagectomy for esophageal cancer in our hospital between January 2009 and December 2011. There were no significant differences in gender, diagnosis, ASA score, occurrence of intraoperative hemorrhage >500 mL, diabetes, and FEV1% >75% between the NPPV group and the IPPV group. The baseline characteristics of the two groups are shown in Table 1. Thirty patients avoided intubation after application of NPPV (30/64, 48.4%), and the mean length of ICU stay in the NPPV patients was 11.5 days. Repeat bronchoscopic treatments effectively solved the problem of decreased ability of airway self-clearance, and the frequency of bronchoscopic treatments in the NPPV group averaged 1.8/day. Sixteen patients failed NPPV and were converted to IPPV. Predetermined criteria for endotracheal intubation after NPPV trial included failure to maintain PaO_2 >65 mmHg with FiO_2 ≤0.6 and persistent dyspnea, tachypnea, and activation of accessory respiratory muscles; need for urgent endotracheal intubation to manage copious tracheal secretions or protect the airways (i.e., coma or neurological disturbances); intolerance of NPPV (i.e., pain, discomfort, or claustrophobia); and hemodynamic instability. The average time to conversion to IPPV was 3.82±7.23 days. The 16 patients were converted to IPPV because of hemodynamic instability, active bleeding, or neurological disturbances.

There were no significant differences in PaO_2/FiO_2 (NPPV 126±31.9 *vs.* IPPV 121±23.4), sequential organ failure

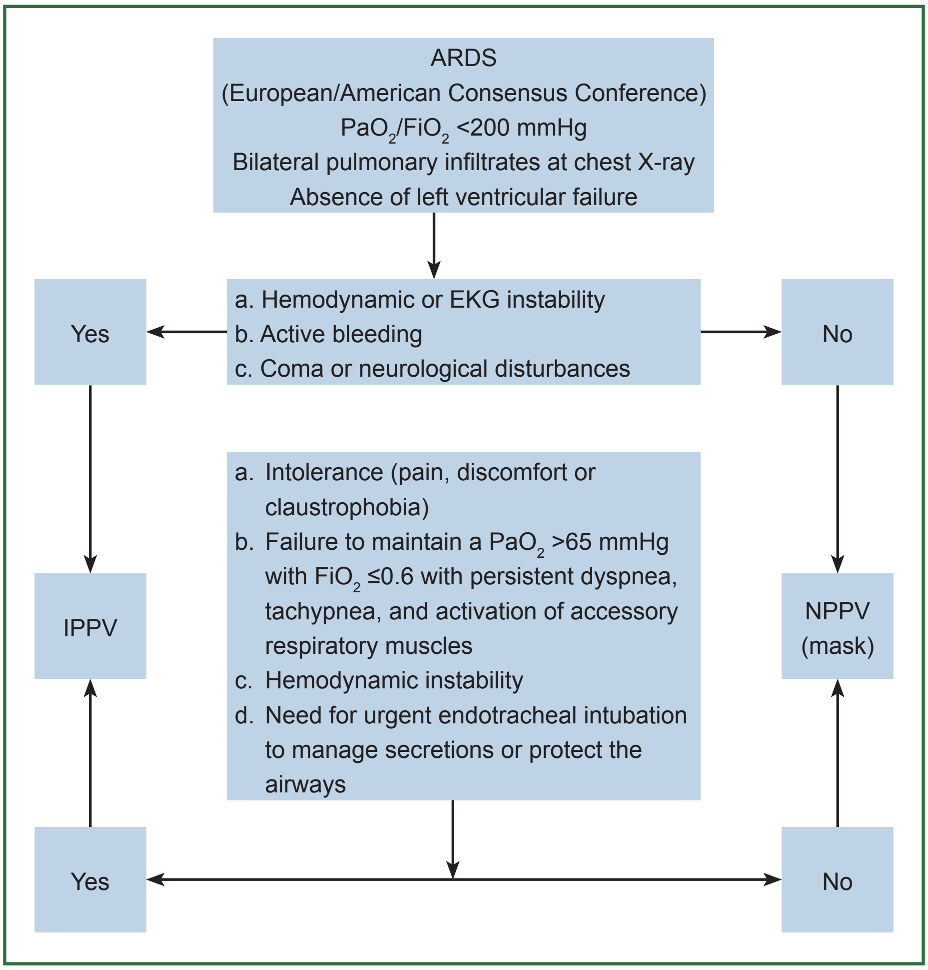

Figure 1. Patients selection. ARDS, acute respiratory distress syndrome; NPPV, noninvasive positive pressure ventilation; IPPV, invasive positive pressure ventilation.

Table 1. General data of 64 ARDS/ALS patients with difficult expectoration.

	n (%)		P value
	NPPV group	IPPV group	
Gender			0.162
Male	31 (96.9)	28 (87.5)	
Female	1 (3.1)	4 (12.5)	
Diagnosis			0.391
Esophageal cancer	28 (87.5)	30 (93.75)	
Cardial cancer	4 (12.5)	2 (6.25)	
ASA score			0.641
ASA-I	30 (93.75)	29 (90.6)	
ASA-II	2 (6.25)	3 (9.4)	
Intraoperative hemorrhage >500 mL	0	0	1
Diabetes	2 (6.25)	3 (9.4)	0.641
FEV1% >75%	31 (96.9)	30 (93.75)	0.554

FEV1%, forced expiratory volume in one second.

assessment (SOFA) score (NPPV 4.3±0.63 *vs.* IPPV 4.4±0.71), or acute physiology and chronic health evaluation (APACHE-II) score (NPPV 21.3±3.58 *vs.* IPPV 20.9±4.21) at the time of onset between the two groups ($P>0.05$), nor were there significant differences in SOFA (NPPV 4.2±0.61 *vs.* IPPV 4.5±0.82) or APACHE-II scores (NPPV 22.1±3.66 *vs.* IPPV 23.6±3.21) between the two groups at 24 h after treatment ($P>0.05$). However, there were significant differences in PaO_2/FiO_2 at 2 h (NPPV 182±29.8 *vs.* IPPV 165±25.5, $P<0.01$) and 24 h (NPPV 207±35.5 *vs.* IPPV 174±28.5, $P<0.05$) after treatment between the two groups. There were no significant differences in 28-day fatality or PaO_2/FiO_2 at the time of onset, nor any significant differences in SOFA or APACHE-II scores at 2 and 24 h after treatment ($P>0.05$).

The mean length of ICU stay for patients in the NPPV group was lower than in the IPPV group (11.5 *vs.* 33.1, $P<0.05$), and the actual fatality rate in the NPPV group was significantly lower than in the IPPV group (6.25% *vs.* 25%, $P<0.05$). The 24-h PaO_2/FiO_2 was significantly improved in the NPPV group *vs.*

the IPPV group (207±35.5 *vs.* 174±28.5 mmHg, P<0.05), and the mean number of major surgery-related complications was significantly smaller (1.25±0.58 *vs.* 2.13±0.81, P<0.01). When patients with ≥2 surgery-related complications were excluded, there was no significant difference in actual fatalities between the two groups (3.22%, 1/31 *vs.* 3.84%, 1/26; P>0.05) (Tables 2,3 and Figure 2).

Discussion

NPPV is an effective option for the treatment of ARF that can avoid endotracheal intubation or tracheotomy. According to the 2006 guidelines for the diagnosis and treatment of ALI/ARDS in China, there is not sufficient evidence to support NPPV as routine treatment for acute hypoxic respiratory failure due to ARDS/ALI, and NPPV is not suitable for patients with increased secretion, decreased ability of airway self-clearance, and a recent history of esophageal surgery. However, a retrospective meta-analysis of trials of NPPV for the treatment of ALI/ARDS between 1995 and 2009 showed that the success rate was about 50%, and suggested that NPPV could be safely be applied in appropriate cases under close supervision (23). In the present study, NPPV was successful in 30 of 32 patients in the NPPV group and the mean length of ICU stay was 11.5 days. Our clinical observations indicated that multiple repeat bronchoscopic treatments could effectively solve the problem of decreased ability of airway self-clearance, with the patients in the NPPV group averaging 1.8 bronchoscopic treatments daily. Thus, esophageal surgery may not be an absolute contraindication for NPPV. Considering that 16 of 32 patients in our series who required IPPV for ARDS after esophagectomy had also received NPPV treatment previously, the overall success rate of NPPV was 64.6%, and the NPPV success rate in ARDS was 48.4%. It could therefore be concluded that NPPV is a good treatment option in appropriate cases and can minimize trauma to these patients.

Studies by Antonelli *et al.* (25) and Yoshiida *et al.* (26) showed that there was no significant difference in PaO_2/FiO_2 between NPPV success groups and NPPV failure groups in the initial stage. However, as PaO_2/FiO_2 improved continuously after treatment in the NPPV success group, it was considered an independent factor for predicting failure of NPPV in the treatment of ALI (26). Antonelli *et al.* (25) also proposed that PaO_2/FiO_2 OI ≤175 at 1 h after NPPV was an independent factor for predicting failure of NPPV for the treatment of ALI. Likewise, we found no significant difference in PaO_2/FiO_2 between IPPV and NPPV groups in the initial stage, but significant differences at 2 (P<0.01) and 24 h (P<0.05) between the two groups, indicating that PaO_2/FiO_2 might be a predictor for success or failure of NPPV treatment. Intra-group comparison in the present study (NPPV 182±29.8 *vs.* IPPV 165±25.5) suggested that PaO_2/FiO_2 >180 at 2 h after treatment is a feasible indicator for continuation with NPPV treatment. Of course, this conclusion needs to be confirmed by more data.

After patients with ≥2 major surgery-related complications were excluded, there was no significant differences in actual fatalities between the two groups (3.22%, 1/31 *vs.* 4%, 1/25; P>0.05). Thus, IPPV may be the best first choice for ARDS patients with ≥2 major surgery-related complications after esophageal surgery, and in such cases, early oral intubation or tracheostomy is required.

In the NPPV group, the 24-h PaO_2/FiO_2 was significantly improved as compared with the IPPV group (207±35.5 *vs.* 174±28.5 mmHg, P<0.05), and the mean number of major surgery-related complications was significantly smaller (NPPV 1.25±0.58 *vs.* IPPV 2.13±0.81, P<0.01). We speculated that the pathological conditions might have been a factor in the relatively larger number of patients with major surgery-related complications in the IPPV group.

In summary, NPPV can be an effective option for the treatment of ARDS/ALI following esophagectomy

Table 2. Evaluation and observation measures: PaO_2/FiO_2, SOFA score, APACHE-II score.

	NPPV group	IPPV group
PaO_2/FiO_2 (h_0) mmHg	126 (±31.9)	121 (±23.4)
PaO_2/FiO_2 (h_2) mmHg	182 (±29.8)	165 (±25.5)**
PaO_2/FiO_2 (h_{24}) mmHg	207 (±35.5)	174 (±28.5)*
SOFA score (h_0)	4.3 (±0.63)	4.4 (±0.71)
SOFA score (h_{24})	4.2 (±0.61)	4.5 (±0.82)
APACHE-II score (h_0)	21.3 (±3.58)	20.9 (±4.21)
APACHE-II score (h_{24})	22.1 (±3.66)	23.6 (±3.21)

*P<0.05, **P<0.01; APACHE, acute physiology and chronic health evaluation; SOFA, sequential organ failure assessment.

Table 3. Evaluation and observation measures: 28-day fatality, actual fatality, and number of surgery-related complications.

Group	28-day fatality (%)	Actual fatality (%)	Fatality excluding cases with ≥2 major post-operative complications	Number of post-operative complications
NPPV	6.25 (2/32)	6.25 (2/32)	3.2% (1/31)	1.25±0.58
IPPV	21.9 (7/32)	25 (8/32)*	3.8% (1/26)	2.13±0.81**

*P<0.05, **P<0.01.

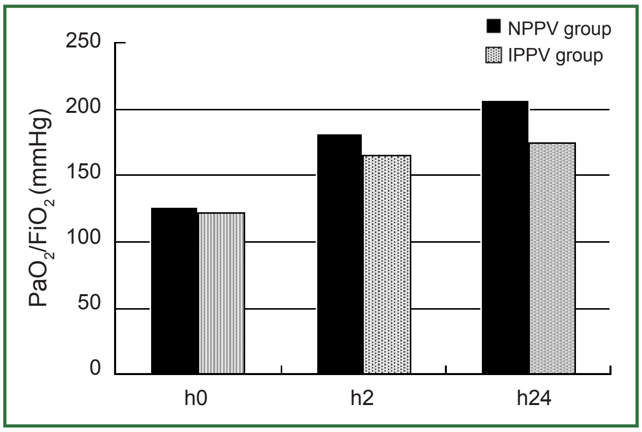

Figure 2. PaO_2/FiO_2 at onset, 2 h and 24 h after NPPV treatment.

for esophageal cancer in select patients, with recurrent bronchoscopic therapy to address the problem of decreased ability of airway self-clearance. However, in patients with two or more severe postoperative complications, including acute renal failure and cardiac arrest, and those with PaO_2/FiO_2 <180 at 2 h after NPPV treatment, invasive mechanical ventilation is required.

Acknowledgements

This study was funded by National Natural Science Foundation of China (Grant Numbers: 81200038, 81170491) and Foundation for Young Talents of Guangzhou Education Bureau (Grant Number: 10A152).

Disclosure: The authors declare no conflict of interest.

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Cite this article as: Yu KY, Zhao L, Chen Z, Yang M. Noninvasive positive pressure ventilation for the treatment of acute respiratory distress syndrome following esophagectomy for esophageal cancer: a clinical comparative study. J Thorac Dis 2013;5(6):777-782. doi: 10.3978/j.issn.2072-1439.2013.09.09