

Effects of lung protective ventilation on postoperative pulmonary outcomes for prolonged oral cancer combined with free flap surgery

Chia-Dan Cheng, DDS^a, Wei-Lin Lin, MD^b, Yuan-Wu Chen, DDS, PhD^a, Chen-Hwan Cherng, MD, PhD^{b,*}

Abstract

The intraoperative lung protective ventilation with low tidal volume, positive end expiratory pressure (PEEP) and intermittent lungs recruitment was found to decrease postoperative pulmonary complications. In this retrospective medical records study, we investigated the effects of lung protective ventilation on postoperative pulmonary outcomes among the patients received prolonged oral cancer combined with free flap surgery.

We collected the medical records of the patients received oral cancer surgery with the operation time more than 12 hours from January 2011 to December 2015. We recorded

1. the patients' characteristics, past medical history, and laboratory data;
2. intraoperative peak airway pressure, fluid intake, urine output, blood loss, and operation duration;
3. postoperative PaO₂/FiO₂ (P/F) ratio when arrived at intensive care unit (ICU), infiltration on Chest X-ray (CXR), duration of ventilator use, ICU stay and hospital stay.

Fifty nine cases were included. Thirty cases received the lung protective ventilation and 29 cases received conventional ventilation. Compared to the patients received conventional ventilation, the patients received intraoperative lung protective ventilation showed

1. higher postoperative P/F ratio (556.6 ± 115.2) vs 341.9 ± 72.7 , $P < .001$);
2. lower incidence of infiltration on postoperative CXR (23.3% vs 51.7%, $P = .047$);
3. shorter duration of ventilator use (6.2 ± 4.5 vs 12.8 ± 7.5 days, $P < .001$); and
4. shorter duration of ICU stay (9.4 ± 5.3 vs 17.1 ± 8.3 days, $P < .001$).

In conclusion, for the prolonged oral cancer combined with free flap surgery, the intraoperative lung protective ventilation improves postoperative pulmonary outcomes and decreases the duration of ICU stay.

Abbreviations: CXR = chest X-ray, ICU = intensive care unit, P/F ratio = PaO₂/FiO₂ ratio, PEEP = positive end expiratory pressure.

Keywords: lung protective ventilation, oral cancer surgery, prolonged anesthesia, pulmonary outcome

Editor: Somchai Amorniyotin.

This work was funded by the grant of TSGH-C106-084 from Tri-Service General Hospital, Taipei, Taiwan.

No conflicts of interest declared.

^aDepartment of Dentistry, ^bDepartment of Anesthesiology, Tri-Service General Hospital and National Defense Medical Center, Taipei, Taiwan.

*Correspondence: Chen-Hwan Cherng, Department of Anesthesiology, Tri-Service General Hospital and National Defense Medical Center, #325, Section 2, Chengkung Road, Neihu 114, Taipei, Taiwan (e-mail: cherng1018@yahoo.com.tw).

Copyright © 2020 the Author(s). Published by Wolters Kluwer Health, Inc. This is an open access article distributed under the terms of the Creative Commons Attribution-Non Commercial License 4.0 (CCBY-NC), where it is permissible to download, share, remix, transform, and buildup the work provided it is properly cited. The work cannot be used commercially without permission from the journal.

How to cite this article: Cheng CD, Lin WL, Chen YW, Cherng CH. Effects of lung protective ventilation on postoperative pulmonary outcomes for prolonged oral cancer combined with free flap surgery. *Medicine* 2020;99:5(e18999).

Received: 4 September 2019 / Received in final form: 26 November 2019 / Accepted: 2 January 2020

<http://dx.doi.org/10.1097/MD.00000000000018999>

1. Introduction

Mechanical ventilation during general anesthesia may cause postoperative pulmonary complications.^[1] Setting a tidal volume higher than 10 ml/kg was used to prevent atelectasis and hypoxemia in the traditional way,^[2] however, many clinical studies have suggested that high tidal volume ventilation leads to alveolar over-inflation, and ventilator-induced lung injury.^[3,4] Animal experiments have also found that high tidal volume ventilation contributes to acute lung injury in healthy lungs.^[5] A lung protective mechanical ventilation, combination of low tidal volume, positive end-expiratory pressure (PEEP), and lungs recruitment maneuver, was initially applied in patients with acute lung injury and acute respiratory distress syndrome and it reduced morbidity and mortality.^[6,7] The lung protective ventilation was later used for surgery under general anesthesia in patients with normal lungs. Many clinical randomized controlled trials have found that the lung protective ventilation significantly decreased the postoperative pulmonary complications among abdominal, cardiovascular, and thoracic surger-

ies.^[8–11] However, there was no data regarding the effectiveness of lung protective ventilation on long duration operation.

The objective of this study was to examine the effect of lung protective ventilation compared with conventional ventilation on the postoperative pulmonary function and outcomes among patients receiving prolonged anesthesia for oral cancer combined with free flap reconstruction surgery.

2. Methods

The study protocol was approved by the Institutional Review Board of Tri-Service General Hospital (TSGHIRB No.: 1-105-15-147). Informed consent was not required because this was a retrospective medical records study. Medical records of patients who received oral cancer combined with free flap reconstruction surgery at a single medical center between January 2011 and December 2015 were collected. The lung protective ventilation for oral cancer combined with free flap surgery was started at February 2014 in our hospital. Only the cases with operation time more than 12 hours were included. The included patients were free of pulmonary morbidity, such as asthma, pneumonia, or chronic obstructive pulmonary disease. Inhalational general anesthesia with desflurane or sevoflurane was conducted. The lung protective ventilation during operation was defined as the combination of low tidal volume (6–8 ml/kg of the predicted body weight), PEEP 5 to 6 cmH₂O and a lungs recruitment maneuver (inspiratory pressure maintained at 30 cmH₂O for 30 seconds) in every 30 minutes. The conventional ventilation was set as 10 to 12 ml/kg of the predicted body weight for tidal volume. The respiration rates of all the patients were set as to maintain the end-tidal CO₂ within 35 to 40 mmHg. Postoperatively, intravenous infusion of dexmedetomidine was administered for analgesia and sedation in ICU. Intravenous fentanyl was rescued for intolerable pain.

We recorded

1. the demographic data, preoperative risk index for postoperative pulmonary complications,^[12] past medical history, and laboratory data, preoperatively;
2. peak airway pressure, fluid intake, urine output, blood loss, and operation duration, intraoperatively;
3. PaO₂/FiO₂ (P/F) ratio and body temperature when arrived at intensive care unit (ICU), infiltration on Chest X-ray (CXR), duration of ventilator use, ICU and hospital stay, postoperatively.

The primary pulmonary outcomes included postoperative lung function presented as P/F ratio, incidence of infiltration on postoperative CXR, and duration of ventilator use. The secondary outcomes included the duration of ICU and hospital stays.

We compared the recorded data between the patients with and without using lung protective ventilation during anesthesia. Statistical analysis was performed by *t* test and Chi-Squared test for continuous and categorical variables, respectively. A *P* value less than .05 was considered as significant difference.

3. Results

A total of 68 medical records were collected initially. Nine cases were excluded due to not met inclusion criteria. Thus, 59 patients, 30 cases received lung protective ventilation and 29 cases received conventional mechanical ventilation, were included for further

Table 1

Patients' characteristics, preoperative and intraoperative data.

Characteristics and variables	Protective ventilation (n = 30)	Conventional ventilation (n = 29)	<i>P</i> value
Age (Y/O)	54.1 ± 9.0	57.9 ± 8.4	.09
Sex (M/F)	25/5	27/2	.449
BW (kg)	62.1 ± 6.6	60.7 ± 5.4	.377
BH (cm)	165.0 ± 5.9	167.2 ± 5.2	.135
Physical status			.960
ASA II, n (%)	21 (70)	19 (66)	
ASA III, n (%)	9 (30)	10 (34)	
Preoperative risk index, n (%)			.962
Risk class 2	19 (63)	17 (59)	
Risk class 3	11 (37)	12 (41)	
Hypertension, n (%)	10 (33)	15 (51)	.244
DM, n (%)	7 (23)	3 (10)	.326
Smoking, n (%)	29 (97)	29 (100)	.986
Preoperation			
Hgb (g/dl)	13.8 ± 1.5	13.2 ± 1.3	.107
WBC (<4,000 or >11,000), n (%)	0 (0)	0 (0)	1.0
Cr (mg/dl)	0.93 ± 0.18	0.89 ± 0.16	.371
AST (U/L)	29.1 ± 8.0	28.4 ± 5.8	.703
ALT (U/L)	31.6 ± 9.0	35.2 ± 7.6	.103
Albumin (g/dl)	3.15 ± 0.29	3.02 ± 0.28	.08
Intraoperation			
Peak air P (cmH ₂ O)	18.6 ± 3.9	23.1 ± 2.2	<.001
Crystalloid (ml)	6613.3 ± 1374.8	6105.2 ± 1239.0	.142
Colloid (ml)	836.7 ± 228.2	827.6 ± 241.9	.882
Urine output (ml)	1086.3 ± 221.0	1043.8 ± 179.8	.422
Blood loss (ml)	711.3 ± 214.9	800.7 ± 143.9	.066
Duration (hr)	14.3 ± 2.6	12.6 ± 1.9	.006

Data are mean ± SD or number of patient (percent).

ALT = alanine aminotransferase, ASA = American Society of Anesthesiology, AST = aspartate aminotransferase, BH = body height, BW = body weight, Cr = creatinine, DM = diabetes mellitus, Hgb = hemoglobin, Peak Air P = peak airway pressure.

analysis. The patients' characteristics, preoperative risk index, medical history, and preoperative laboratory data were not different between 2 groups (Table 1). Intraoperatively, the intake/output, blood loss, and duration of operation were comparable between 2 groups (Table 1). Compared to the patients received conventional mechanical ventilation, the patients received lung protective ventilation showed

1. lower intraoperative peak airway pressure (18.6 ± 3.9 vs 23.1 ± 2.2 cmH₂O, *P* < .001);
2. higher postoperative P/F ratio (556.6 ± 115.2 vs 341.9 ± 72.7, *P* < .001);
3. lower incidence of infiltration on postoperative CXR (23.3% vs 51.7%, *P* = .047);
4. shorter duration of ventilator use (6.2 ± 4.5 vs 12.8 ± 7.5 days, *P* < .001); and
5. shorter duration of ICU stay (9.4 ± 5.3 vs 17.1 ± 8.3 days, *P* < .001) (Table 2). The length of hospital stay was not different between groups.

4. Discussion

This study found that, compared to the conventional high tidal-volume mechanical ventilation, the protective lung ventilation during operation improved postoperative pulmonary outcomes

Table 2
Postoperative data.

Variables	Protective ventilation (n=30)	Conventional ventilation (n=29)	P value
Postoperation			
PaO ₂ /FiO ₂ Ratio	556.6±115.2	341.9±72.7	<.001
BT (°C)	35.6±0.5	35.8±0.6	.169
Infiltration on CXR, n (%)	7 (23.3)	15 (51.7)	.047
On ventilator time (day)	6.2±4.5	12.8±7.5	<.001
ICU Stay (day)	9.4±5.3	17.1±8.3	<.001
Hospital stay (day)	29.2±7.3	30.8±10.3	.493

Data are mean ± SD or number of patient (percent).

BT = body temperature, CXR = chest X-ray, ICU = Intensive Care Unit.

in patients received a prolonged anesthesia for oral cancer combined with free flap surgery. Just like the abdominal, cardiovascular, and thoracic surgeries, the intraoperative lung protective ventilation may also benefit the long duration operation.

There was ample evidence from clinical and experimental studies demonstrated that conventional high tidal volume mechanical ventilation leads to lung injury for both diseased and healthy lungs.^[3,5,13] The possible mechanisms included direct mechanical trauma of the alveoli (barotrauma or volutrauma) and subsequent release of cytokine mediators from alveolar epithelium into the systemic circulation (biotrauma).^[14–18] The lung protective ventilation (low tidal volume with PEEP and intermittent lungs recruitment) has been applied in many kinds of surgeries and led to decrease postoperative pulmonary complications and improve pulmonary outcomes.^[8–11] Several meta-analyses have evaluated the effect of lung protective ventilation compared with conventional high tidal volume ventilation on surgical patients with normal lungs. Intraoperative lung protective ventilation resulted in decrease of pulmonary infections, atelectasis, acute lung injury, and the need for postoperative mechanical ventilation.^[19–21] This beneficial result of the lung protective ventilation has also been shown in experimental studies. Maria et al and Camilo et al both groups found that variable ventilation combined with lungs recruitment maneuver decreased lung tissue damage and pulmonary inflammation in rats.^[22,23]

The lung protective ventilation has been used for many kinds of surgeries and resulted in an improvement of postoperative pulmonary outcomes. However, there was no report to examine the effect of intraoperative lung protective ventilation on the long duration surgery. In this study, long duration operations with more than 12 hours were investigated and an identical result as the other surgeries was obtained. Compare to the conventional mechanical ventilation, the intraoperative lung protective ventilation resulted in better postoperative pulmonary outcomes that included higher P/F ratio when the patient arrived at ICU, lower incidence of infiltration on postoperative CXR, and shorter duration of ventilator use. The results of this study are not unexpected. Based on the possible mechanisms of the conventional ventilation-induced lung injury (baro-, volu-, and bio-trauma), the longer the conventional high tidal volume ventilation use, the severer the lungs being damaged. In addition, minimal hemodynamic fluctuation occurred during the second half of the operation when free flap reconstruction was performing. Under such steady condition, a low tidal volume

with PEEP and intermittent lungs recruitment supposed to be the appropriate mode to mechanical ventilation. No wonder a big difference of the duration of ventilator use and ICU stay between the 2 groups was founded in this study.

There are some limitations to this study. First, this is a retrospective observational study. Potential bias, such as patient's preoperative medical conditions, may exist. Second, the sample size is not large enough. However, statistical analysis of our data showed a significant difference between groups. A prospective randomized control trial is indicated to verify the effectiveness of lung protective ventilation on postoperative pulmonary outcomes for patients receiving prolonged surgery.

5. Conclusion

Compare to high tidal volume ventilation without PEEP, the intraoperative lung protective ventilation with low tidal volume, PEEP and intermittent lungs recruitment improves postoperative pulmonary outcomes and decreases the duration of ICU stay for the prolonged oral cancer combined with free flap surgery.

Author contributions

Chia-Dan Cheng contributed to the data collection, data analysis, and manuscript preparation. Wei-Lin Lin and Yuan-Wu Chen contributed to the data collection and analysis. Chen-Hwan Cheng contributed to all aspects of this manuscript, including conception and design, data analysis and interpretation, manuscript writing

References

- Fernandez-Bustamante A, Frenzl G, Sprung J, et al. Postoperative pulmonary complications, early mortality, and hospital stay following noncardiothoracic surgery: a multicenter study by the perioperative research network investigators. *JAMA Surg* 2017;152:157–66.
- Wrigge H, Pelosi P. Tidal volume in patients with normal lungs during general anesthesia: lower the better? *Anesthesiology* 2011;114:1011–3.
- Lellouche F, Dionne S, Simard S, et al. High tidal volumes in mechanically ventilated patients increase organ dysfunction after cardiac surgery. *Anesthesiology* 2012;116:1072–82.
- Tremblay LN, Slutsky AS. Pathogenesis of ventilator-induced lung injury: trials and tribulations. *Am J Physiol Lung Cell Mol Physiol* 2005;288:L596–8.
- De Prost N, Costa EL, Wellman T, et al. Effects of ventilation strategy on distribution of lung inflammatory cell activity. *Crit Care* 2013;17:R175.
- Petrucci N, De Feo C. Lung protective ventilation strategy for the acute respiratory distress syndrome. *Cochrane Database Syst Rev* 2013;2:CD003844.
- Putensen C, Theuerkauf N, Zinserling J, et al. Meta-analysis: ventilation strategies and outcomes of the acute respiratory distress syndrome and acute lung injury. *Ann Intern Med* 2009;151:566–76.
- Futier E, Constantin JM, Paugam-Burtz C, et al. A trial of intraoperative low-tidal volume ventilation in abdominal surgery. *N Engl J Med* 2013;369:428–37.
- Sundar S, Novack V, Jervis K, et al. Influence of low tidal volume ventilation on time to extubation in cardiac surgical patients. *Anesthesiology* 2011;114:1102–10.
- Severgnini P, Selmo G, Lanza C, et al. Protective mechanical ventilation during general anesthesia for open abdominal surgery improves postoperative pulmonary function. *Anesthesiology* 2013;118:1307–21.
- Güldner A, Kiss T, Serpa Neto A, et al. Intraoperative protective mechanical ventilation for prevention of postoperative pulmonary complications: a comprehensive review of the role of tidal volume, positive end-expiratory pressure, and lung recruitment maneuvers. *Anesthesiology* 2015;123:692–713.
- Arozullah AM, Khuri SF, Henderson WG, et al. Development and validation of a multifactorial risk index for predicting postoperative pneumonia after major noncardiac surgery. *Ann Intern Med* 2001;135:847–57.

- [13] Imai Y, Parodo J, Kajikawa O, et al. Injurious mechanical ventilation and endorgan epithelial cell apoptosis and organ dysfunction in an experimental model of acute respiratory distress syndrome. *JAMA* 2003;289:2104–12.
- [14] Gurkan OU, O'Donnell C, Brower R, et al. Differential effects of mechanical ventilatory strategy on lung injury and systemic organ inflammation in mice. *Am J Physiol Lung Cell Mol Physiol* 2003;285:L710–8.
- [15] Tojo K, Nagamine Y, Yazawa T, et al. Atelectasis causes alveolar hypoxia-induced inflammation during uneven mechanical ventilation in rats. *Intensive Care Med Exp* 2015;3:56.
- [16] Plötz FB, Slutsky AS, van Vught AJ, et al. Ventilator-induced lung injury and multiple system organ failure: a critical review of facts and hypotheses. *Intensive Care Med* 2004;30:1865–72.
- [17] Pelosi P, Negrini D. Extracellular matrix and mechanical ventilation in healthy lungs: back to baro/volutrauma? *Curr Opin Crit Care* 2008;14:16–21.
- [18] Lionetti V, Recchia FA, Ranieri VM. Overview of ventilator-induced lung injury mechanisms. *Curr Opin Crit Care* 2005;11:82–6.
- [19] Gu WJ, Wang F, Liu JC. Effect of lung-protective ventilation with lower tidal volumes on clinical outcomes among patients undergoing surgery: a meta-analysis of randomized controlled trials. *CMAJ* 2015;187:E101–9.
- [20] Tao T, Bo L, Chen F, et al. Effect of protective ventilation on postoperative pulmonary complications in patients undergoing general anaesthesia: a meta-analysis of randomized controlled trials. *BMJ Open* 2014;4:e005208.
- [21] Yang D, Grant MC, Stone A, et al. Meta-analysis of intraoperative ventilation strategies to prevent pulmonary complications is low tidal volume alone sufficient to protect healthy lungs? *Ann Surg* 2016;263:881–7.
- [22] Maia LA, Samary CS, Oliveira MV, et al. Impact of different ventilation strategies on driving pressure, mechanical power, and biological markers during open abdominal surgery in rats. *Anesth Analg* 2017;125:1364–74.
- [23] Camilo LM, Motta-Ribeiro GC, de Ávila MB, et al. Variable ventilation associated with recruitment maneuver minimizes tissue damage and pulmonary inflammation in anesthetized lung-healthy rats. *Anesth Analg* 2018;127:784–91.