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Original Article

The association of ventilator-associated pneumonia with the frequent exchange of endotracheal tube

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Abstract: Background: In endotracheal intubated patients, the prolonged presence of an endotracheal tube (ETT) and mechanical ventilation support is associated with increased risk of ventilator associated pneumonia (VAP). The aim of this study was to investigate whether it is safe to prolong the use of the endotracheal tube without causing an increase in the incidence of VAP in patients under long term mechanical ventilator support. Materials and methods: Eleven prolonged mechanical ventilation (PMV) patients were recruited from respiratory care wards (RCW) and divided into two groups by randomized complete block design. ETT was changed either every 30 days (control group) or 90 days (experiment group). The incidence of VAP and cumulative rate of patients remaining free of VAP were assessed. Results: A total of 48 times of ETT changes were completed in 11 patients. The incidence of VAP were 8.8% (3/34 times) in the control group and 42.9% (6/14 times) in the experiment group (P = 0.01). The cumulative rate of patients remaining free of VAP probability was higher in the group of routinely changed every 30 days during the study period (P = 0.002). There were no statistically significant differences between the two groups including microorganisms that caused VAP, disease severity classification at VAP onset, transferred to ICU and hospital mortality. Conclusions: Routine 30-day change of ETT could reduce the incidence of VAP but it should be weighed on the possible risk of airway trauma during the invasive procedure.

Keywords: Ventilator associated pneumonia, endotracheal tube, tube exchange

Introduction

Ventilator associated pneumonia (VAP) is a serious nosocomial infection that develops 48 hours after the initiation of mechanical ventilation support and occurs in about 20% of critically ill patients [1, 2]. It is associated with high morbidity and mortality rate in these patients and substantially increased in medical expenditure [3, 4]. Therefore, effective strategies to reduce the incidence of VAP have always been an importance issue.

In the care of intubated patients, endotracheal tube (ETT) are routinely changed every 30 days because of the following concerns: 1) increased VAP incidence if prolonged use, 2) tube blocking from excessive secretions and 3) tracheal mucosa injury by ETT material degenerate and cuff pressure change. In an observational study, bacterial biofilm formation from multiple organisms has been demonstrated on ETT surfaces in the microscopic images [5, 6]. Once formed, biofilm is inherently resistant to many antimicrobial agents and lead to a local hydrolysis. Physical detachment of the biofilm could cause deep pulmonary infection [7]. Abud et al. also found histological damages in the scanning electron micrographs of the tracheal mucosa in ETT cuff region which included rarefaction of cilia, epithelial rupture with disorganization and cell loss. These could induce ring-shaped tracheitis and circumferential fibrous stenosis [8, 9].

Prolonged mechanical ventilation (PMV), is defined as those who require ventilator support for at least 6 hours a day and continued for more than 21 days [10]. In Taiwan, it is estimated that about 18-25% of the PMV patients refuse to accept tracheostomy [11-13]. Prolonged presence of an ETT in mechanical ventilated patients could increase the risk of aspiration of contaminated oropharyngeal secretions into the lung, which might contribute to tracheal colonization and increase the risk of VAP [14]. However, the risk and difficulty when facing an ETT change, especially in patients with difficult airway remains a challenge for many intensivists. Furthermore, the dangerous of airway injury and introducing endogenous oropharyngeal bacteria to patient's lower airway during the insertion of an ETT are also major drawbacks. When an ETT should be changed is still based on clinician's discretion in Taiwan and remains a dilemma in clinical practice.

In the tracheostomy tube exchange, manufacturers enclose their recommendations for routine changes the polyvinyl chloride (PVC) tubes every 29 days. In clinical experience, PVC tubes may be used for 3-4 months before they became stiffen was suggested in the guideline [15, 16]. Furthermore, "too" frequent changes of the tube may give rise to traumatic effects such as causing stoma to stretch, especially with a cuffed tube, creation of a false passage into the anterior mediastinum, bleeding at the tracheostomy site, and substantial discomfort [15]. In addition, Bahng et al. disclosed that reuse of the tracheostomy tube was correlated with a higher incidence of pneumonia, whereas the frequency of tube change and age did not [17].

To our knowledge, there's no evidence available for the optimal time of exchanging ETT in patients receiving long-term mechanical ventilator support. In this study, we would like to known whether it is safe to prolong the use of the ETT without causing an increase incidence of VAP in patients under PMV support.

Materials and methods

Study population

This study was conducted during the period between Sep 2010 and Mar 2012 at three RCWs in Taichung, Taiwan. A total of 11 patients who received PMV support via oral endotracheal tubes were recruited in this study. Patients were divided into two groups by randomized complete block design, five were in the control group and six were in the experimental group. Endotracheal tubes equipped with drainage of subglottic secretions (Hi-Lo Evac tube; Mallinckrodt Medical, Athlone, Ireland) were used in this study. For the controlled group, ETT was routinely changed every 30 days and ETT change was prolonged to once every 90 days in the experimental group. The study was approved by the Institutional Review Board of CSMUH (IRB No.CS09129) and informed consent was received from every subject.

VAP prevention strategies

The strategies of VAP prevention routinely used in each participating center, including enteral delivery of nutritional support via NG tubes, maintained in semi-recumbent body position, subglottic secretions used intermittent suctioning for 10 to 15 s with a suction pressure of 100 to 150 mmHg before endotracheal sputum suction and maintain subglottic suction port effectiveness [18], patient's oral cavity was cleaned with chorhexidine and cuff pressure maintained between 25 and 30 cm H_2O and checked every 8 hours.

Diagnostic criteria for VAP

The diagnosis of VAP was based on the American Thoracic Society (ATS) guidelines [1]. The diagnostic criteria included mechanical ventilation for at least 48 hrs, a new or progressive radiographic infiltrate plus at least two of the followings: fever (body temperature >38°C), purulent tracheal secretions, leukocytosis or leukopenia, (leukocyte count >10,000/μL or <4000/μL). Only patients with a positive semi-quantitative bacterial culture (SQ-EAs) ≥ moderate growth from the endotracheal aspirate were included in the VAP subjects [19]. Patients were excluded if they were <20 years of age, unstable hemodynamic status, newly appearance of lung infiltrative lesions that is compatible with pneumonia, and sepsis at the time of screening for eligibility.

Data collection

Patients' baseline characteristics including age, gender, severity of illness index asses-

Table 1. Clinical and demographic details of patients at study enrolment

Characteristics	Total (n = 11)	30 days exchange (n = 5)	90 days exchange (n = 6)	*p* value
Age (yrs)	75.73 ± 11.99	79.60 ± 5.23	72.50 ± 15.44	0.54
Male gender	3 (27.3%)	2 (40.0%)	1 (16.7%)	0.55
Glasgow Coma Scale	7.55 ± 2.02	8.40 ± 1.52	6.83 ± 2.23	0.33
APACHE II	21.36 ± 0.61	20.40 ± 0.68	22.17 ± 0.87	0.24
SAPS II	44.00 ± 2.86	44.20 ± 3.83	43.83 ± 2.14	0.79
SOFA scores	4.82 ± 1.60	4.80 ± 0.84	4.83 ± 2.14	0.66
Coesxisting illnesses				
Pulmonary	5 (45.5%)	2 (40.0%)	3 (50.0%)	1.00
Cardiac	10 (90.9%)	4 (80.0%)	6 (100%)	0.46
Liver	1 (9.1%)	1 (20.0%)	0 (0.0%)	0.46
Renal	1 (9.1%)	0 (0.0%)	1 (16.7%)	1.00
Diabetes mellitus	8 (72.7%)	4 (80.0%)	4 (66.7%)	1.00
Cerebral vascular accident	6 (54.5%)	4 (80.0%)	2 (33.3%)	0.24
Other	2 (18.2%)	0 (0.0%)	2 (33.3%)	0.46
Reason for mechanical ventilation				
Neurologic failure	5 (45.5%)	2 (40.0%)	3 (50.0%)	1.00
Acute respiratory failure	4 (36.4%)	1 (20.0%)	3 (50.0%)	0.55
Heart failure	2 (18.2%)	1 (20.0%)	1 (16.7%)	1.00
Sepsis	2 (18.2%)	1 (20.0%)	1 (16.7%)	1.00
Cardiac arrest	5 (45.5%)	1 (20.0%)	4 (66.7%)	0.24
Miscellaneous	1 (9.1%)	0 (0.0%)	1 (16.7%)	0.55

APACHE II, Acute Physiology and Chronic Health Evaluation; SAPS II, Simplified Acute Physiology Score; SOFA, Sequential Organ Failure Assessment Score; discrete variables are expressed as counts (%) and continuous variables as mean ± SE. *p* value <0.05 was considered significant in patients of 30 days exchange vs 90 days exchange subjects.

sed by Acute Physiology and Chronic Health Evaluation (APACHE II), Simplified Acute Physiology Score (SAPS II) and Sequential Organ Failure Assessment (SOFA) score, reasons for mechanical ventilation support and coexisting illnesses. Moreover, ventilator and physiological variables of patients at study enrolment were recorded. The following variables potentially influencing the occurrence of VAP were also recorded: previous surgery, regular hemodialysis, stress ulcer prophylaxis, use of sedative drugs and paralytic agents, antibiotic therapy, and frequency of humidifier and ventilator circuits change. The primary outcome was the incidence of VAP and cumulative rate of patients remaining free of VAP. Secondary outcomes included the severity criteria at VAP onset, transferred to ICU, hospital mortality (follow up until 90-days after end of study) and the cause of death.

Statistical analysis

Continuous value was expressed as the mean ± SE and the categorical variables were expressed as percentages. Comparability of groups was analyzed by the Mann-Whitney *U* test, chi-square test with the Fisher exact test, as suitable. The cumulative rate of remaining free of VAP in the two groups were examined by the Kaplan-Meier method and compared by log-rank test. Statistical analysis was performed using the IBM SPSS Statistics v20 (Armonk, NY). A $P<0.05$ was considered statistically significant.

Results

Eleven patients were recruited into this study including five were in the control group and six were in the experimental group. Clinical and demographic characteristics are summarized in **Table 1**, including age, gender, severity of illness index, reasons for mechanical ventilation support and coexisting illnesses. There were no significant differences in the characteristics in both groups.

Ventilation and physiological variables are shown in **Table 2**. The ventilation variables

Table 2. Ventilation and physiological variables of patients at study enrolment

	Total (n = 11)	30 days exchange (n = 5)	90 days exchange (n = 6)	*p* value
Ventilation variables				
Tidal volume, ml	544.91 ± 47.80	540 ± 41.83	549.00 ± 55.91	1.00
Respiratory rate /min	13.18 ± 2.40	13.80 ± 2.49	12.67 ± 2.42	0.79
PEEP, cmH_2O	5.55 ± 1.04	6.20 ± 1.30	5.00 ± 0.00	0.13
FIO_2, %	34.09 ± 6.64	32.00 ± 4.47	35.83 ± 8.01	0.43
PaO_2/FIO_2, mmHg	418.27 ± 155.24	420.80 ± 145.44	416.17 ± 176.83	1.00
Arterial pH	7.45 ± 0.54	7.47 ± 0.15	7.44 ± 0.72	0.79
$PaCO_2$, mmHg	37.26 ± 4.91	38.58 ± 2.72	36.17 ± 6.25	0.13
RSBI, breaths/min/L	203.87 ± 87.68	174.52 ± 63.53	228.33 ± 102.79	0.18
Physiological variables				
White blood cells, 10^{-9}/L	9894.55 ± 1859.55	9772.00 ± 2012.83	9996.67 ± 1909.74	1.00
Hemoglobin, g/L	8.93 ± 1.66	8.42 ± 1.75	9.36 ± 1.61	0.18
Albumin, gm%	3.17 ± 0.47	3.08 ± 0.46	3.25 ± 0.51	0.54

PEEP, positive end-expiratory pressure; FIO_2, inspired oxygen fraction; PaO_2/FIO_2, Ratio of the partial pressure of oxygen in arterial blood (PaO_2) to the inspired oxygen fraction (FIO_2); RSBI, rapid shallow breathing index; continuous variables as mean ± SE. *p* value <0.05 was considered significant in patients of 30 days exchange vs 90 days exchange subjects.

Table 3. Variables potentially influencing ventilator-associated pneumonia during study period

	Total (n = 11)	30 days exchange (n = 5)	90 days exchange (n = 6)	*p* value
Previous surgery	4 (36.4%)	1 (20.0%)	3 (50.0%)	0.55
Regular hemodialysis	1 (9.1%)	0 (0.0%)	1 (16.7%)	1.00
Stress ulcer prophylaxis				
Proton pump inhibitor	2 (18.2%)	2 (40.0%)	0 (0.0%)	0.18
Antacid	5 (45.5%)	1 (20.0%)	4 (66.7%)	0.24
H2 receptor antagonists	2 (18.2%)	2 (40.0%)	0 (0.0%)	0.18
Sucralfate	0 (0.0%)	0 (0.0%)	0 (0.0%)	
Intravenous sedation	1 (9.1%)	0 (0.0%)	1 (16.7%)	1.00
Paralytic agents	0 (0.0%)	0 (0.0%)	0 (0.0%)	
prior administration of antibiotics	9 (81.8%)	5 (100.0%)	4 (66.7%)	0.46
Frequency of humidifier changes	6.05 ± 1.26	6.30 ± 2.04	5.83 ± 1.73	0.93
Frequency of ventilator circuits changes	6.05 ± 1.26	6.30 ± 2.04	5.83 ± 1.73	0.93

Discrete variables are expressed as count (%) and continuous variables as mean ± SE. *p* value <0.05 was considered significant in patients of 30 days exchange vs 90 days exchange subjects.

included tidal lung volume, respiratory rate, PEEP level applied, FiO_2, PaO_2/FiO_2 ratio, $PaCO_2$, blood gas analysis and weaning indices; while the physiologic variables included WBC count, hemoglobin and albumin level. There were no significant differences in both groups.

In **Table 3**, factors which could potentially cause VAP during the study period including previous surgery, whether patient was receiving regular hemodialysis, stress ulcer prophylactic treatment, intravenous sedation, muscle paralytic agents, prior administration of antibiotic treatment within 90 days, frequency of ventilator circuits and humidifier changes were recorded. There were also no significant differences found between the two study groups.

The incidence of VAP is presented in **Table 4**. The total numbers of ETT changes were 48 times, and were mostly performed in the control group [34 (70.8%)] as compared with the experiment group [14 (29.2%)]. VAP was microbiologically confirmed in 9 episodes and VAP was significantly less frequent in the control group [3 (8.8%)] than the experiment group [6 (42.9%); $P = 0.01$]. All the incidences of VAP were late onset type. There was no signifi-

Table 4. Incidence of ventilator-associated pneumonia

	Total (n = 11)	30 days exchange (n = 5)	90 days exchange (n = 6)	*p* value
No. of ETTT exchange	48 (100%)	34 (70.8%)	14 (29.2%)	
Incidence of VAP with clinical criteria	9 (18.8%)	3 (8.8%)	6 (42.9%)	0.01
Early-onset VAP	0	0	0	
Late-onset VAP	9 (18.8%)	3 (8.8%)	6 (42.9%)	0.01
Prior duration of MV (d)	622.18 ± 109.69	683.80 ± 141.48	570.83 ± 172.10	0.79

p value <0.05 was considered significant in patients of 30 days exchange vs 90 days exchange subjects.

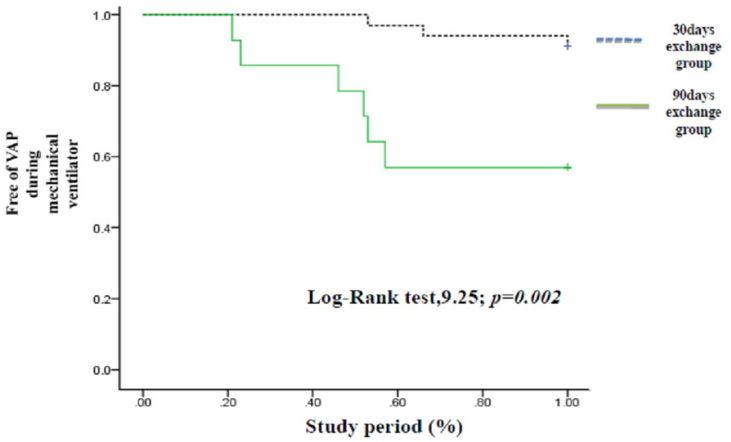

Figure 1. Kaplan-meier analyses of cumulative rate of patients remaining free of VAP. The cumulative rate of patients remaining free of VAP probability was better in the group of routinely exchanged every 30 days during the study period (log-rank test, *P* = 0.002).

cant difference in the duration of mechanical ventilation support between the study groups. The probability of remaining free of VAP during study period was significantly higher in the control group (log-rank test, 9.25; *P* = 0.002) (**Figure 1**). Among the 9 episodes of VAP, 6 (66.7%) were monomicrobial. *Haemophilius influenza* was the most frequently yielded microorganism [5 (55.6%)] (**Table 5**).

The severity criteria at VAP onset including the incidence of bacteraemia, septic shock, death and transferred to ICU were not significantly different between the two groups (**Table 6**). Hospital mortality (follow up until 90 days after end of study) was 60.0% in the control group and 66.7% in the experiment group (*P* = 1.00) and there were no differences in the cause of death.

Discussion

Our results suggested that routine ETT changes at a monthly interval, when compared to those of 3-month prolonged use, were likely to reduce the incidence of VAP and extended VAP free day in the PMV patients. To our knowledge, current study is the first to evaluate the relationship between endotracheal tube change and VAP.

As advances in critical care techniques, many of the critical ill patients could survive but remained dependent on ventilator support and resulted in the state of chronic critical illness [20]. It is estimated that between 4-13% of mechanical ventilated patients require PMV [21]. Previous studies showed that up to 20% of the critical ill patients were remained in ventilator dependent status and only about 5% of these patients were able to wean [22, 23]. These patients often require long period of intensive care and consume a disproportionately large share of total medical expense [24, 25]. The increased burden on the medical cost has driven many countries to develop step down units. Establishing a weaning unit would potentially reduce overall treatment costs was reported in a retrospective cohort study conducted in the UK [21]. In the 1990s, changes in reimbursement have created incentives for acute care hospitals to transfer these patients from ICU to long term assisted care facilities (LTAC) [26]. In Taiwan, the ventilator dependent care is divided into 4 stages according to the integrated delivery system [27] designed by the national health institute bureau (NHIB) in 2000. Stage 1 intensive care unit [28], includes difficult to wean patients and could stay up to 21 days. Stage 2 respiratory care center (RCC), includes prolonged mechanical ventilator dependent patients and could stay up to 42 days.

Table 5. Isolated pathogens in patients of ventilator-associated pneumonia

Bacteria	Total (n = 9)	30 d exchange (n = 3)	90 d exchange (n = 6)	*p* value
Monomicrobial VAP	6 (66.7%)	3 (100.0%)	3 (50.0%)	0.24
Polymicrobial VAP	1 (11.1%)	0 (0.0%)	1 (16.7%)	0.67
Organisms				
P. aeruginosa	1 (11.1%)	0 (0.0%)	1 (16.7%)	0.67
Haemophilus influenzae	5 (55.6%)	3 (100.0%)	2 (33.3%)	0.12
Enterobacter aerogens	1 (11.1%)	0 (0.0%)	1 (16.7%)	0.67
Streptococcus group G	1 (11.1%)	0 (0.0%)	1 (16.7%)	0.67

Data are expressed as number (percentage). *p* value <0.05 was considered significant in patients of 30 days exchange vs 90 days exchange subjects.

Table 6. Secondary outcome in all patients

Characteristics	Total (n = 11)	30 d exchange (n = 5)	90 d exchange (n = 6)	*p* value
Severity criteria at VAP onset				
Bacteremia	1 (9.1%)	0 (0.0%)	1 (16.7%)	1.00
Septic shock	2 (18.2%)	1 (20.0%)	1 (16.7%)	1.00
Death	2 (18.2%)	1 (20.0%)	1 (16.7%)	1.00
Transferred to ICU	2 (18.2%)	1 (20.0%)	1 (16.7%)	1.00
Hospital mortality with 90 days[a]	7 (63.6%)	3 (60.0%)	4 (66.7%)	1.00
Causes to death				
Septic shock	5 (45.5%)	2 (40.0%)	3 (50.0%)	1.00
ARDS	1 (9.1%)	0 (0.0%)	1 (16.7%)	1.00
Renal failure	1 (9.1%)	0 (0.0%)	1 (16.7%)	1.00
Heart failure	1 (9.1%)	1 (20.0%)	0 (0.0%)	0.46

Discrete variables are expressed as count (%); with 90 days[a], Follow up until 90 days after end of study. *p* value <0.05 was considered significant in patients of 30 days exchange vs 90 days exchange subjects.

Stage 3 RCW, also included prolonged mechanical ventilator dependent patients who failed to wean from ventilator support at RCC and could stay until they are successfully weaned from ventilator. Stage 4, home ventilator care, includes prolonged mechanical ventilator dependent patients who are in stable condition and could be discharged home [22]. Our study was conducted in three RCWs locating in central Taiwan.

Tracheostomy is usually performed in patients with weaning difficulties and prolonged need of ventilator support. In a multicentre study included the population of ventilator dependent patients admitted to long-term care hospitals for weaning from mechanical ventilation. The percentage of patients who received tracheostomy was 94.7% and more than 90% of patients had at least three penetrating indwelling tubes/catheters [20]. Tracheostomy rate in Taiwan varies but is significantly lower than many other countries. The low percentage of tracheostomy rate in Taiwan is presumably being attributed to the cultural influence and traditional factors. The general acceptability of tracheostomy among both patients and their family is low and the misleading concept of tracheostomy is probably from limited and incorrect information they received. Therefore, a certain number of patients who needed chronic mechanical ventilator support remained prolong indwell with an endotracheal tube. In these patients, when an ETT should be changed is still inconclusive. To our knowledge, current study is the first to evaluate the optimal time of exchanging ETT in patients receiving long-term mechanical ventilator support.

The challenge of changing of an ETT is high when compared with a tracheostomy tube, particularly in patients with difficult airway. Patients are required to be heavily sedated and paralyzed before intubation. Complications may occur during laryngoscopy particularly in patients with difficult intubation. The risk of airway injury, aspiration of gastric contents, bronchospasm, hypoxic brain injury and unrecognized esophageal intubation could occur during the procedure. Airway exchange catheters (AEC) may be helpful in these situations, these hollow polyvinyl chloride ventilating catheters can be inserted through a ETT and left in situ when the ETT is removed and then these catheters provide a ready means of re-intubating the trachea [28]. Many experts recommend the use of AEC in difficult tube exchange [29-31]. Therefore, appropriate to

use of AEC might be able to diminish related injuries in routine ETT exchange.

Airway mucociliary clearance and cough reflex could be impaired in the presence of an endotracheal tube. Tracheobronchial secretions would be accumulated and thus increase the risk of pneumonia. The insertion of an endotracheal tube could also induce airway injury and introduce endogenous oropharyngeal bacteria to the lower respiratory tract. VAP is likely related to aspiration of the contaminated secretions which was colonized with the pathogenic bacteria in patient's aerodigestive tract [32]. Aspiration of oropharyngeal bacteria around the endotracheal tube cuff and into the lower respiratory tract could occur. Aspiration of subglottic secretion by using a specifically designed endotracheal tube has been proved by several studies and could reduce the incidence of VAP incidence [33-35]. Endotracheal tubes equipped with dorsal opening that allows for drainage of subglottic suction were employed in our study.

There are several limitations in our study. First, our enrolled patient number was small. Patients who remained intubated and needed chronic mechanical ventilator support are usually limited in each RCW. Most of these vulnerable patients were usually associated with serious and complicated comorbidities such as cardiovascular disease, chronic lung disease, renal failure, hepatic function impairment, cerebrovascular disorder, diabetes mellitus and malignancies. Many patients were thus excluded from this study or refused to participate because of their unstable clinical condition and the safety concern of their attending physicians. Second, the diagnosis of VAP was made on the discretion of the in charging pulmonologist which mostly relied on chest roentgenography findings and clinical signs, so misdiagnosis could exit. However, it was often difficult to detect a new or progressive pulmonary infiltrate that superimposed on the chronic lung infiltrate in many of our ventilator dependent patients. Furthermore, the optimal diagnostic approaching is difficult in patients with VAP. Endotracheal aspiration with semi-quantitative culture of the aspirate was adopted in our study for the diagnosis of VAP. It was also employed as the diagnostic techniques for VAP in several studies [19]. The clinical outcomes and overall use of antibiotics were similar in both BAL with quantitative culture of BAL fluid and endotracheal aspiration with semi-quantitative culture of the aspirate. Third, bias could exit because it was impossible to blind the participated physicians in patient allocation in our study.

In conclusion, routine ETT changes at monthly interval, when compared with those of 3-month prolonged use, were likely to reduce the incidence of VAP and extend VAP free day in PMV patients. However, the benefit of monthly ETT changes should be weighed on the risk of airway trauma during the invasive procedure.

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Disclosure of conflict of interest

None.

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