

# Repositioning of endotracheal tube and risk of ventilator-associated pneumonia among adult patients: A matched case-control study

Taha Ismaeil<sup>1,2</sup>, Latifah Alfunaysan<sup>1</sup>, Nouf Alotaibi<sup>1</sup>, Shatha Alkadi<sup>1</sup>, Fatmah Othman<sup>2,3</sup>

<sup>1</sup>Department of Respiratory Therapy, College of Applied Medical Sciences, King Saud Bin Abdulaziz University for Health Science, <sup>2</sup>King Abdullah International Medical Research Center, <sup>3</sup>Research Unit, College of Applied Medical Sciences, King Saud Bin Abdulaziz University for Health Science, Riyadh, Saudi Arabia

#### Address for correspondence:

Dr. Fatmah Othman, Research Unit, College of Applied Medical Sciences, King Saud Bin Abdulaziz University for Health Science, Riyadh, Saudi Arabia.  
E-mail: othmanf@ksau-hs.edu.sa

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#### Abstract:

**INTRODUCTION:** Ventilator-associated pneumonia (VAP) is one of the most serious hospital-acquired infections to occur among mechanically ventilated patients. Many risk factors for VAP have been identified in the literature; however, there is a lack of studies examining the association between endotracheal tube (ETT) repositioning and an increase in the risk of VAP. The aim of the present study, therefore, was to investigate the effect of ETT repositioning and the risk of developing VAP.

**METHODS:** Matched case-control studies were conducted among mechanically ventilated patients admitted to the intensive care unit (ICU) at King Abdulaziz Medical City from 2016 to 2018. Patients who had a documented VAP diagnosis were identified and matched to four controls (within a 10-year age band). The history of ETT repositioning (defined as changes in the positioned ETTs from the first reading at the time of ETT insertion) was explored in the medical files of the sample, as were other demographic and comorbidity risk factors. Logistic regression analysis was used to test the association between ETT repositioning and VAP.

**RESULTS:** A total of 24 cases were identified with documented VAP diagnosis during the study. Those cases were matched to 81 controls. The mean age was 55 (standard deviation 21) for both cases and controls. VAP patients had a greater history of ETT repositioning (46%) compared to controls (29%). Patients who had a history of ETT repositioning were twice as likely to develop VAP as patients who had no history of ETT repositioning ( $P = 0.13$ ). After adjustment of a potential confounder, the results showed evidence of an increased risk of VAP after ETT repositioning (odds ratio 3.1, 95% confidence interval 1.0–9.6).

**CONCLUSION:** Reposition of ETT considers as a risk factor for VAP in ICU patients, and appropriate measures should be applied to reduce movements of the ETT tube.

#### Keywords:

Endotracheal tube, mechanical ventilation, ventilator-associated pneumonia

Ventilator-associated pneumonia (VAP) is one of the most serious hospital-acquired infections to occur among mechanically ventilated patients.<sup>[1]</sup> The American Thoracic Society and Infectious Diseases Society of America jointly define VAP as “a pneumonia in patients with mechanical ventilation for at least 48 h and

characterized by the presence of a new or progressive infiltrate, signs of systemic infection (temperature and blood cell count), changes in sputum characteristics, and detection of the causative agent.”<sup>[2]</sup> Over the years, the incidence of VAP has decreased; however, many reports have estimated this incidence to be between 10% and 20%.<sup>[1,3,4]</sup> Some of the evidence has reported that VAP is associated with an increase in

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mortality rate, prolonged mechanical ventilation, and health-related costs.<sup>[1,5]</sup>

The presence of an endotracheal tube (ETT) is closely related to the occurrence of VAP.<sup>[1]</sup> The postulated pathophysiological mechanism suggests that an ETT may inhibit mucociliary clearance, interfere with cough reflex, and damage trachea surface, thus allowing bacteria to enter the lower respiratory tract rapidly.<sup>[1,6-8]</sup>

In clinical practice, the depth of the ETT is determined by performing chest X-ray immediately after intubation. If the tip of ETT is too deep or too shallow, the clinician readjusts its position.<sup>[9-11]</sup> Such movements of the ETT are often unavoidable, creating opportunities for aspiration and therefore increasing the risk of VAP. Given the uncertainty regarding the possible link between VAP and ETT repositioning, we aimed in this study to address the association between ETT repositioning and the increase in the risk of VAP in mechanically ventilated patients in intensive care unit (ICU). We anticipated that the findings of this research would help clinicians and respiratory therapists to better understand the association between VAP and ETTs, and to set a preventive measurement that ensures correct ETT positioning.

## Methods

### Study design and setting

A matched case-control study was conducted at King Abdulaziz Medical City, Riyadh, Saudi Arabia between 2016 and 2018. Data from the hospital's ICU, which include many specialized critical care units,<sup>[12]</sup> were utilized for this study. In the ICU, a multidisciplinary team follows the recommended guidelines and strategies for VAP prevention. Since 2015 the hospital has utilized an electronic medical recording system for all patients, within which all health information is recorded, including diagnosis (using the International Classification of Diseases-10 [ICD-10] classification), laboratory results, radiological reports, procedures, referrals, and any medical prescriptions. Within these records, the respiratory therapist usually documents any information regarding ETT manipulation and repositioning as text in each patient electronic file. The study period (2016–2018) was chosen to reduce the effect of misclassification bias for our exposure definition as well as to enhance the ascertainment of the VAP diagnosis using these medical records.

### Study participants and data collection

In this study, cases were adult patients aged >16 years intubated for >48 h and with a confirmed diagnosis of VAP (defined as ICD code diagnosis). The definition of VAP in the hospital usually relies on three criteria: radiological findings, signs of ongoing infection, and

laboratory results. Controls were randomly selected from all patients who were intubated for >48 h using the ICU data and up to four controls were matched to each case on age (10-year age band). The selection of controls was made without replacement. Based on the previous literature, VAP occurs between 28% and 32% of patients who receive mechanical ventilation.<sup>[1]</sup> We have calculated the sample size needed for this study considering effect size equal to 3 (odds ratio [OR] = 3) with 32% as a percentage of exposure among the controls.<sup>[13]</sup> Thus, we needed to include 24 VAP cases to detect a three-fold increase in the risk of VAP with  $\alpha = 0.05$  and 80% powers if we matched 1 case to 4 controls.<sup>[13]</sup>

A data collection sheet was used to extract information about the selected patients from their electronic medical records. The information included demographics, body mass index (normal, overweight, and obese), date of intubation, date of VAP diagnosis, the reason for intubation (categorized into general categories: respiratory failure, coma, and injury), and type of ICU. The injury category includes those patients who have been involved in any type of injuries such as road traffic accident and fall and have been intubated as a result of this injury. ETT repositioning was defined in our study as any difference between two readings of ETT level and was obtained from medical records. The first reading is that performed immediately after intubation, while the second is obtained within 48 h of intubation. Furthermore, we collected information on clinical comorbidities, assessed using the Charlson Comorbidity Index score,<sup>[14]</sup> which is a method of categorization of comorbidities of patients consisting of 19 conditions, including congestive heart failure, peripheral vascular disease, diabetes, diabetes with diabetic complications, chronic pulmonary disease, mild and severe liver disease, hemiplegia, renal disease, leukemia, lymphoma, metastatic tumor, and acquired immunodeficiency syndrome. We categorized the scores into four categories as follows: 0 (no comorbidities), 1–2 (mild), 3–4 (moderate), and  $\geq 5$  (severe).

This study was approved by the King Abdullah International Medical Research Center IRB Approval Committee (protocol number SP18/224/R).

### Statistical analysis

The patients' characteristics for both cases and controls were compared using the Chi-square test for categorical variables if one or more of cells have an expected frequency of five or more. Otherwise Fisher's exact test was used, and we used an unpaired *t*-test for continuous variables. Conditional logistic regression was used to estimate OR with 95% confidence intervals (CIs) for the risk of VAP. Each potential confounder that significantly associated with outcome in the univariate regression analysis has been entered in the model. Then, variables

that have been included in the logistic regression model were selected based on a 10% change in the OR of the association between ETT repositioning and VAP. Data were analyzed in STATA version 15 (StataCorp LLC, College Station, TX, USA).

### Results

A total of 24 cases were identified as having a documented VAP diagnosis during the study. Majority of the cases were matched (within a 10-year age band) to 81 controls, whereas only six VAP cases have <4 controls due to a limited number of eligible controls in the data, therefore, the total number of 105 patients were included in the analysis. The mean age was 55 year (standard deviation [SD] 23) for cases where the mean age for controls was 55 years (SD 21). Around 19 (79%) of the cases were male patients, compared to 58 (72%) in the control group. Characteristics of cases and controls matched for age are presented in Table 1. Compared with the controls, VAP was more likely to occur in surgical ICU – 37% cases versus 12% of their matched controls,– which difference was statistically significant ( $P < 0.05$ ). Comorbidity was higher in the

control group compared to patients with VAP. Coma was the most common diagnosis for ICU admission among both cases and their matched controls.

VAP patients had more history of ETT repositioning (46%) compared to controls (29%). Patients who had a history of ETT repositioning were twice as likely to develop VAP as patients who had no history of ETT repositioning ( $P = 0.13$ ) [Table 2]. After adjustment of potential confounders (gender, comorbidity, and ICU diagnosis), the results of the adjusted analysis showed evidence of an increased risk of VAP after ETT repositioning (OR 3.1, 95% CI 1.0–9.6).

### Discussion

The findings of our research suggest that cases exhibited a high risk of developing VAP after ETT repositioning. The increased risk of VAP persisted despite adjustment for the potential confounding effects of gender and comorbidity.

#### Comparison with other studies

Although the exact etiology for developing VAP is still unknown, many studies have indicated that the

**Table 1: Characteristics of the cases and their matched controls**

Patients characteristics	Number of cases (n=24), n (%)	Number of controls (n=81), n (%)	Crud OR	95% CI
Age (mean, SD)	55 (23.1)	55 (21.8)	NA	NA
ETT size ( mean, SD)	7.2 (0.8)	7.4 (0.4)	NA	NA
Gender				
Male	19 (79)	58 (72)	1	
Female	5 (21)	23 (28)	0.66	0.22-1.98
Type of ICU				
Medical	15 (62)	71 (87)	1	
Surgical	9 (37)	10 (12)	4.26	1.47-12.28
Charlson comorbidity index				
0	5 (21)	21 (26)	1	
1-2	9 (37)	16 (20)	2.36	0.66-8.42
3-4	3 (12)	14 (17)	0.90	0.18-4.38
>5	7 (29)	30 (37)	0.98	0.27-3.51
BMI				
Normal	8 (33)	31 (38)	1	
Overweight	10 (42)	26 (32)	1.49	0.51-4.32
Obese	6 (25)	24 (29)	0.96	0.29-3.16
Reason of intubation				
Respiratory failure	9 (37)	29 (36)	1	
Coma	10 (42)	41 (51)	0.78	0.28-2.17
Injury	5 (21)	11 (13)	1.46	0.40-5.34

CI=Confidence interval, BMI=Body mass index, OR=Odd ratio, SD=Standard deviation, ICU=Intensive care unit, ETT=Endotracheal tube, NA=Not available

**Table 2: Odd ratio and the 95% confidence interval of association between history of endotracheal tube reposition and ventilator-associated pneumonia**

History of ETT repositioning	All patients (%)	Cases (%)	Control (%)	95% CI	
				Un-adjusted OR*	Adjusted OR
No ETT repositioning	70 (66)	13 (54)	57 (70)	1	1
ETT repositioning	35 (33)	11 (46)	24 (29)	2.25 (0.85-5.97)	3.12 (1.01-9.66)

\*OR are adjusted for the gender, comorbidity and ICU diagnosis. ETT=Endotracheal tube. OR=Odd ratio, CI=Confidence interval, ICU=Intensive care unit

interaction of several risk factors in ICU can lead to an increase in patient susceptibility to the development of VAP.<sup>[1,4]</sup> The presence of an ETT is considered the main risk factor for VAP because it impairs natural defense mechanisms, such as the cough reflex and mucociliary clearance, which increase tracheal colonization and the subsequent development of VAP.<sup>[1,15]</sup>

Numerous preventative measures have been introduced to prevent VAP. Some of these preventative strategies include the semirecumbent position, with the head being elevated to 30°–45°,<sup>[16]</sup> using a coated ETT,<sup>[17]</sup> and leakage prevention measurements such as subglottic secretion drainage and ETT cuff modifications.<sup>[1,7]</sup> Although many studies have examined the effectiveness of ETT innovation, less is known about the clinical implications of these measures in the context of the ability of such modifications to prevent VAP.<sup>[1,5,18]</sup> In addition, previous reports have identified some independent factors that could be associated with VAP, including bronchoscopy, tube thoracostomy, tracheostomy, and the severity of diseases.<sup>[3,19]</sup> In our study, comorbidity and the site of intubation were independent risk factors for VAP. In clinical practice, the interaction of those risk factors can put the patient at higher risk. Thus, identifying those factors proves useful in identifying patients at high risk of VAP, as well as in developing further preventive measures.

The risk of developing VAP after ETT repositioning have been discussed in a previous study<sup>[13]</sup> which estimated an undusted OR of 3.1 (95% CI 1.03–9.42), a finding which is consistent with our own. Furthermore, they found that diabetes mellitus and the use of antibiotics on the 1<sup>st</sup> day of intubation were potential protective factors against VAP.<sup>[13]</sup>

### Limitations and strengths

This study has several strengths. By using electronic data to define the VAP in this study, we minimized the effect of measurement bias in our results. Thus, many studies have claimed that the incidence of VAP is overestimated as many researchers have used clinical data to diagnose VAP.<sup>[1,3]</sup> Moreover, in this study, we collected information on comorbidities and causes of admission to ICU to control for any potential confounders; however, many other related factors were not included in our analysis, which may have an impact on the association between VAP and ETT repositioning.<sup>[13]</sup> In the present study, we attempted to overcome the limitations of previous studies by using matching between cases and controls; in addition, the analysis was adjusted to gender and comorbidity to minimize the potential confounding effects of these variables.

We acknowledge certain limitations of this study: we did not have information on certain risk factors for VAP such

as using antibiotics and hence, these were not included in the analysis.<sup>[20]</sup> However, as with any observational studies, the effect of residual confounding in addition to unmeasured confounding cannot be eliminated. Furthermore, not all cases have four controls as in this analysis owing to matching without replacement, and we do not anticipate that will change the direction of our estimation. In addition, we could not determine whether pulling up the ETT or pushing it down was more associated with the risk of VAP. Thus, further study could be designed to examine this to support the pathophysiology mechanism of the association between VAP and ETT repositioning.

### Conclusion

VAP is a multifactorial process and still presents an important challenge to clinicians and respiratory therapists in ICU.<sup>[21]</sup> We showed, in this study, that ETT repositioning could be considered as an established independent risk factor for VAP among ICU patients. The results of this study could help clinicians as well as respiratory therapists to identify patients at high risk of developing VAP. Further research would be needed to determine an effective way to ensure the right depth of ETT and apply measures to reduce the incidence of ETT repositioning.

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### Conflicts of interest

There are no conflicts of interest.

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