Efficacy of Endotracheal Tube Cuff Modification in Preventing Ventilator-associated Pneumonia

Yanshuo Wu, Congcong Zhao, Meirong Sun, Jingjing Bu, Zhenjie Hu and Yanling Yin

Department of Critical Care Medicine, The Fourth Hospital of Hebei Medical University, Hebei, China

ABSTRACT

The aim of this study was to evaluate the effect of modifying the cuff on preventing ventilator-associated pneumonia (VAP). PubMed, Embase and Cochrane Library were systematically searched from inception to April 2022, for randomised controlled trials (RCTs) that compared the effect of a new type of cuff intubation with traditional cuff intubation on VAP incidence and intensive-care unit (ICU) mortality in mechanically ventilated patients. Nine RCTs with 1937 patients were finally evaluated. The pooled results for the incidence of VAP showed that the modified cuff significantly decreased the morbidity of VAP compared with the traditional cuff (relative ratio (RR) = 0.73, 95% confidence interval (CI) 0.56–0.95, p = 0.02). The subgroup analysis revealed that polyurethane (PU) cuff (RR = 0.82, 95% CI 0.46–1.48, p = 0.52), conical cuff (RR = 0.97, 95% CI 0.73–1.28, p = 0.82) and PU-conical cuff (RR = 1.36, 95% CI 0.85–2.18, p = 0.20) did not decrease the incidence of VAP. Moreover, the improved cuff combined with subglottic secretion drainage (SSD) could significantly reduce the VAP incidence (RR = 0.58, 95% CI 0.44–0.77, p = 0.0001). In terms of ICU mortality, there was no statistically significant difference (RR = 0.83, 95% CI 0.68–1.02, p = 0.08) between the two groups. The modified cuff is superior to the traditional cuff in VAP prevention. In particular, the modified cuff combined with subglottic secretion drainage has more advantages.

Key Words: *Ventilator-associated pneumonia, Intubation, Endotracheal cuff, Intensive care unit, Meta-analysis.*

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INTRODUCTION

The mechanically supported patients frequently acquire ventilator-associated pneumonia (VAP) in critical care units (ICUs). Data of 2014 from the National Healthcare Safety Network showed that the incidence of ventilator-associated events, defined as infection-related in the ICU ranged from 2.0-11.9 per 1000 ventilator days.[1] In the WHO Southeast Asian Region, the VAP incidence fluctuated from 2.13-116 per 1000 ventilator days.[2] VAP prolongs the duration of mechanical ventilation by 5.4–21.8 days, the length of ICU stay by 6.1-20.5 days, and the length of hospital stay by 11.0–32.6 days.[3-6] VAP has an attributable mortality of 4.6%–13%.[7,8] A study speculated that hypothetical eradication VAP could result in reduction in ICU mortality of 1.7% by Day 10 and 3.6% by Day 60.[9] The hospitalisation cost for patients with VAP was higher than that for patients without VAP.[3,10,11] Therefore, additional improvements in preventive strategies are still needed to reduce the incidence of VAP and its negative impact.

Correspondence to: Dr. Yanling Yin, Department of Critical Care Medicine, The Fourth Hospital of Hebei Medical University, Hebei, China
E-mail: 1052723646@qq.com

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The respiratory tract loses its normal physiological structure as a result of intubation, and it is exposed to external factors that damage the relatively sterile tract. Oropharyngeal secretions enter the lower respiratory tract through the space between the trachea and trachea intubation tube. Thus, VAP risk is increased.[12] In the order to reduce the movement of secretions downward, tracheal tube cuff seals off the trachea. In conventional cuffs, polyvinyl chloride (PVC) is the typical material which folds easily, creating channels for secretions to pass through.[13,14] In the recent years, modifying the design of endotracheal tube cuffs has been an important intervention to decrease the danger of VAP.

The shape of the cuff has been improved from cylindrical to conical. The principle of the conical cuff is that the tapered cone is consistent with the diameter of the trachea at a certain point. This may offer a zone of full tracheal sealing, preventing the development of longitudinal folds and lowering microaspiration.[15] The improvement of the cuff material is primarily due to the use of polyurethane (PU). The thickness of the PU cuff is 7–10 µm, which is much lower than that of the PVC cuff that has a thickness of 50–70 µm.[16] The thinner the material, the better the fit to the trachea, and the less likely it is to form folds.

Studies *in vitro* have confirmed that cuff modification can effectively reduce liquid leakage.[17-20] Nevertheless, the clinical studies have reported different results. Some previous studies have conducted systematic reviews on tapered cuff and PU cuff.[21-23] However, there are several confounding factors such as

subglottic secretion drainage and PU-conical cuffs, which may increase the risk of bias.

The aim of this study was to summarise the RCTs on improvement of cuff and classify the types of cuff for determining the effectiveness of a modified cuff in the prevention of VAP.

METHODOLOGY

An in-depth literature search was conducted using Embase, PubMed and Cochrane Library from inception to April 2022. A structured search was conducted using medical subject headings (MeSH) and entry terms, including endotracheal tube cuff, tapered cuff, conical cuff, polyurethane cuff, conventional cuff, pneumonia, ventilator-associated. The language of publication was not restricted. In addition, references from reviews, studies, and the internet were manually searched. An ethics committee approval was not required. The protocol was added to the International Platform of Registered Systematic Review and Meta-analysis Protocols (INPLASY 202250018).

Based on the PICOS criteria, participants (P) were mechanically-ventilated, critically-ill adults. Intervention (I) was PU cuff, conical cuff, or other types of cuffs. Control (C) was conventional cuff (HVLP cuff). Primary outcome (O) was the incidence of VAP and study design (S) was randomised controlled trial (RCT). The methods of pneumonia diagnosis and incidence measurement were not restricted. Case reports, retrospective studies, observational studies, letters to the editor, animal studies, and review articles were excluded. Whenever the two reviewers disagreed, a third reviewer was consulted.

The following data were independently extracted from each study by two reviewers. This data included: author, publication year, country, department, number of patients, the cuff type in the experimental group, tracheal tube internal diameter, PEEP, VAP assessment, cuff pressure, and other important clinical outcomes. If further data were required, the trial authors were contacted through e-mail. Discussion with a third reviewer helped to settle any differences in evaluation.

After finalising the selection of literature, two independent reviewers assessed the quality of the literature according to the Cochrane Collaboration's method for assessing any bias. Seven methodological criteria were used to evaluate the selected studies. A funnel plot was not applied due to the low number of studies.

The analysis of data was performed by using Review Manager (Cochrane Collaboration, version 5.3). Mantel-Haenszel model was used to calculate the relative ratio (RR) and 95% confidence interval (CI) for binary variables. I^2 and Chi-square tests were used to assess the heterogeneity among studies, with an I^2 >50% or p <0.1 denoting significant heterogeneity. In cases where heterogeneity was significant, the random effect model was used; if not, the fixed effect model was used. To identify the potential sources of heterogeneity, several sensitivity analyses were performed. A value of $p < 0.05$ was considered to be statistically significant.

RESULTS

Four hundred and twenty related articles were screened based on the database search, 149 of which were excluded for duplication. After reading the title and abstract, 252 articles were omitted. Ten articles were excluded based on full-text review. Finally, the study included nine published RCTs with 1937 patients.[24-32] The flow diagram illustrates the search and exclusion criteria (Figure 1), and the study characteristics are described in Table I. Three studies included multiple modified types of cuff.[27,28,32] To ensure the comparability of the data, all modified cuffs that were different from the traditional cuff were classified into the experimental group.

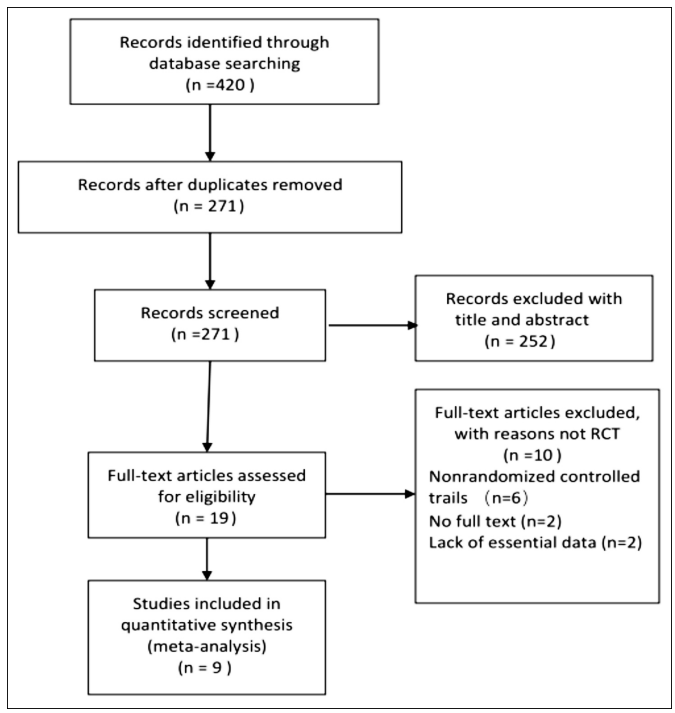

Figure 1: PRISMA flow diagram showing search and selection strategies.

The outcomes of the quality assessment of studies were inputted into the Review Manager software according to the quality assessment judgement criteria, and the results are shown in Figure 2.

Nine studies reported the incidence of VAP. The VAP incidence from 1134 patients with a modified cuff was compared with 803 patients with a conventional cuff. The pooled result for the incidence of VAP revealed that the modified cuff significantly decreased the incidence of VAP in comparison to the traditional cuff (RR = 0.73, 95% CI 0.56–0.95, p = 0.02, Figure 3). A subgroup analysis performed according to the type of cuff showed that the incidence of VAP was not reduced by PU cuff (RR = 0.82, 95% CI 0.46–1.48, p = 0.52, Figure 4), conical cuff (RR = 0.97, 95% CI 0.73–1.28, p = 0.82, Figure 5) and PU-conical cuff (RR = 1.36, 95% CI 0.85–2.18, p = 0.20, Figure 6) in comparison to the traditional cuff. Interestingly, the improved cuff combined with SSD could significantly reduce the incidence of VAP (RR = 0.58, 95% CI 0.44–0.77, p= 0.0001, Figure 7).

Table I: Characteristics of studies included in the meta-analysis.

Studies	Country	Department	No. of patients	Tracheal tube type in experimental group	Internal diameter	Cuff pressure	PEEP	VAP assessment	Duration of follow-up
Deem S 2016	USA	Medical-ICU	102	PU+conical PU+conical+SSD	7mm/F, 7.5mm/M	25-30cmH_2O	NR	Definition of CDC	During ICU stay
Jailette E 2017	France	Mixed-ICU	325	PVC+conical	7.5mm/F, 8.0mm/M	25cmH_2O	>5cmH_2O	Clinical, radiological, microbiological	28 days or ICU discharge
Lorente L 2007	Spain	Mixed-ICU	280	PU+SSD	NR	25cmH_2O	NR	Definition of CDC	During ICU stay
Mahmoodpoo A 2013	Iran	Mixed-ICU	96	PU+ cylindrical+SSD PU+conical+SSD	7-7.5mm/F, 8-8.5mm/M	25-30mmHg	5cmH_2O	Clinical, radiological, microbiological CPIS	During ICU stay
Mahmoodpoo A 2017	Iran	Mixed-ICU	274	PU+Conical+SSD	7-7.5mm/F, 8-8.5mm/M	25-30 mmHg	5cmH_2O	CPIS	During ICU stay
Monsel A 2016	France	Mixed-ICU	109	PVC+Conical	NR	20-30cmH_2O	5.0-6.3cmH_2O	Johanson criteria	28days or during hospital stay
Philippart F 2015	France and Tunisia	Mixed-ICU	604	PVC+conical PU+conical PU+cylindrical	7.5mm /F or 8.0mm/M	25-30cmH_2O	≥5cmH_2O	Clinical, radiological, biological	During ICU stay
Poelaert J 2008	Belgium	Surgical-ICU	134	PU	8mm/F 9mm/M	20-26cmH_2O	<6cmH_2O	Johanson criteria	During hospital stay
Shuhas P 2016	Indian	Surgical-ICU	80	PU	NR	≥25 cm H_2O	NR	CPIS Biological	During ICU stay

DC, Centers for Disease Control and Prevention; CPIS, Clinically infection pulmonary score; F, Females; ICU, Intensive care unit; No, Number; M, Males; PEEP, Positive end-expiratory pressure; PVC, Polyvinyl chloride; PU, Polyurethane; SSD, Subglottic secretion drainage; VAP, Ventilator-associated pneumonia.

Table II: Qualitative analysis of secondary outcome measures.

Studies	Modified cuff and traditional cuff	Duration of mechanical ventilation		ICU length of stay		Hospital length of stay	
		Statistics	p-value	Statistics	p-value	Statistics	p-value
Deem S 2016	PU+conical	5.6±7.2	NS	7.7	NS	19.5	NS
	PU+conical+SSD	6.5±12.7		10.1		23.8	
	Traditional cuff	4.5±4.3		10.2		22.1	
Jailette E 2017	PVC+conical	NR	NR	16(10-26)	0.28	NR	NR
	Traditional cuff			14(9-25)			
Lorente L 2007	PU+SSD	10.5±15.91	0.71	14.1±17.91	0.53	NR	NR
	Traditional cuff	11.1±15.19		15.5±19.93			
Mahmoodpoo A 2013	PU+cylindrical+SSD	NR	NR	18(12-33)	NS	NR	NR
	PU+conical+SSD			17(13-31)			
	Traditional cuff			12(8-22)			
Mahmoodpoo A 2017	PU+Conical+SSD	11.6±7.1	0.71	15±5	0.33	27.2±7.0	0.51
	Traditional cuff	12.3±10.5		18±10		29.5±7.0	
Monsel A 2016	PVC+Conical	27.5(12-306)	0.46	9(5-20)	0.21	20(12-32)	0.91
	Traditional cuff	29(9-97)		7(4-14)		22(13-30)	
Philippart F 2015	PVC+conical	NR	NR	9.5(5-17)	NR	NR	NR
	PU+conical			12(6-19)			
	PU+cylindrical			10.5(5-18)			
	Traditional cuff			11.0(5-18)			
Poelaert J 2008	PU	19±13	0.22	3±5	0.87	16±9	0.53
	Traditional cuff	25±36		3±4		17±11	
Shuhas P 2016	PU	4(3-7.5)	0.25	6(4-8.5)	0.04*	NR	NR
	Traditional cuff	6(4-8)		8(6-11)			

*NS, Not significant; NR, Not reported; PVC, Polyvinyl chloride; PU, Polyurethane; SSD, Subglottic secretion drainage. Continuous data are reported as median (interquartile range) or mean (±SD). * p <0.05.*

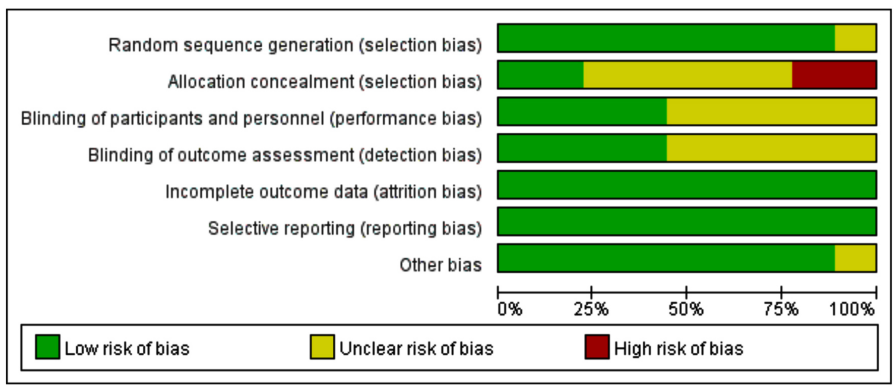

Figure 2: The graph showing a risk of bias.

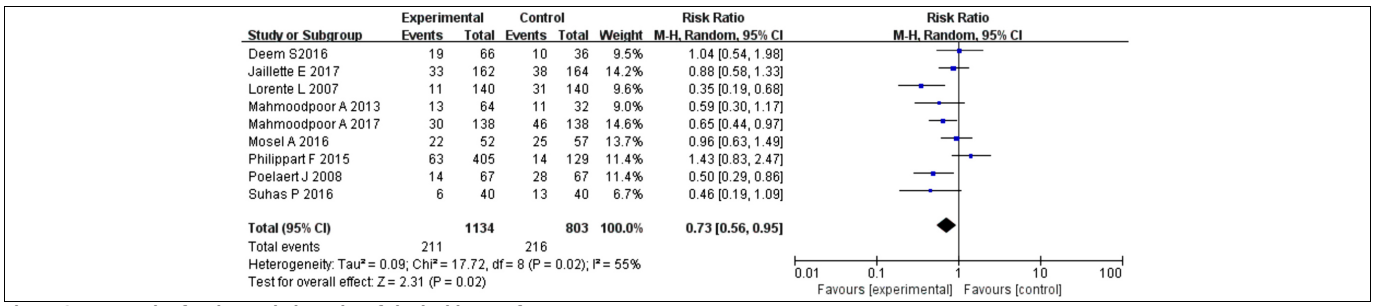

Figure 3: Forest plot for the pooled results of the incidence of VAP.

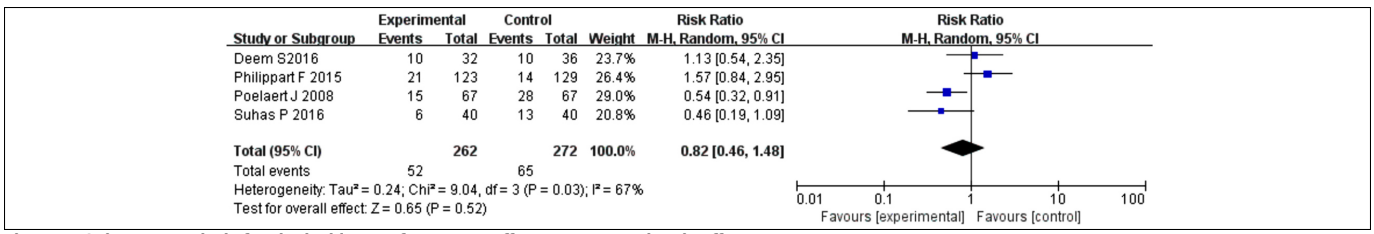

Figure 4: Subgroup analysis for the incidence of VAP; PU cuff *versus* conventional cuff.

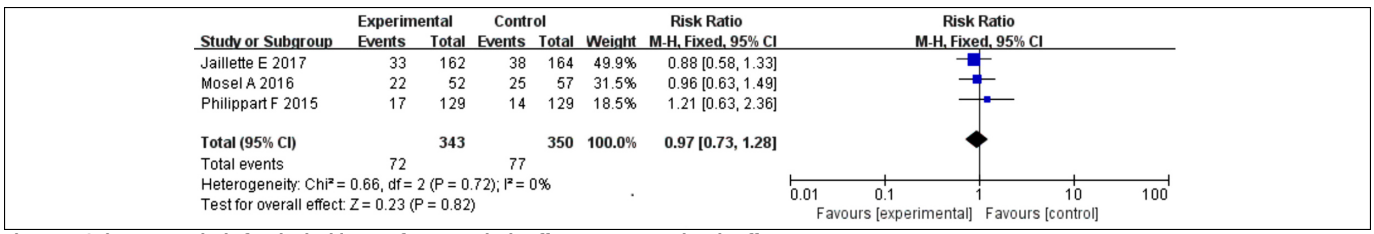

Figure 5: Subgroup analysis for the incidence of VAP; conical cuff *versus* conventional cuff.

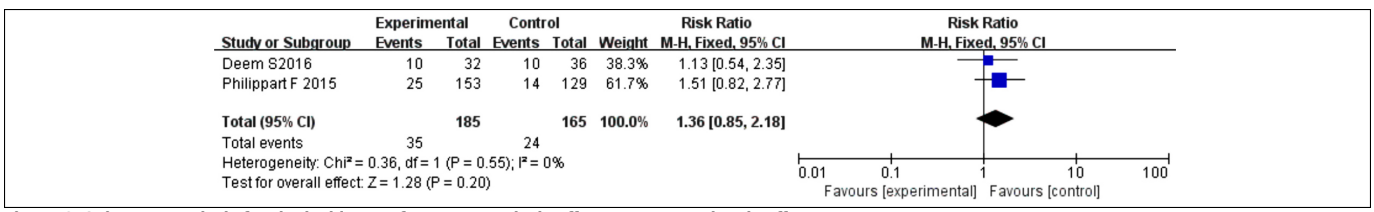

Figure 6: Subgroup analysis for the incidence of VAP; PU-conical cuff *versus* conventional cuff.

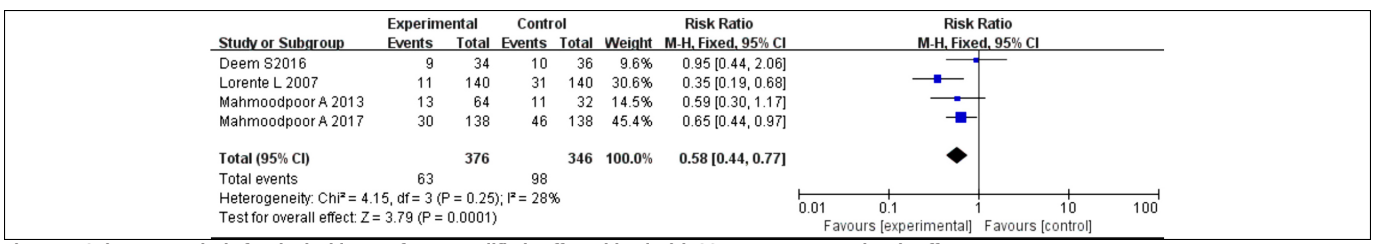

Figure 7: Subgroup analysis for the incidence of VAP; modified cuff combined with SSD *versus* conventional cuff.

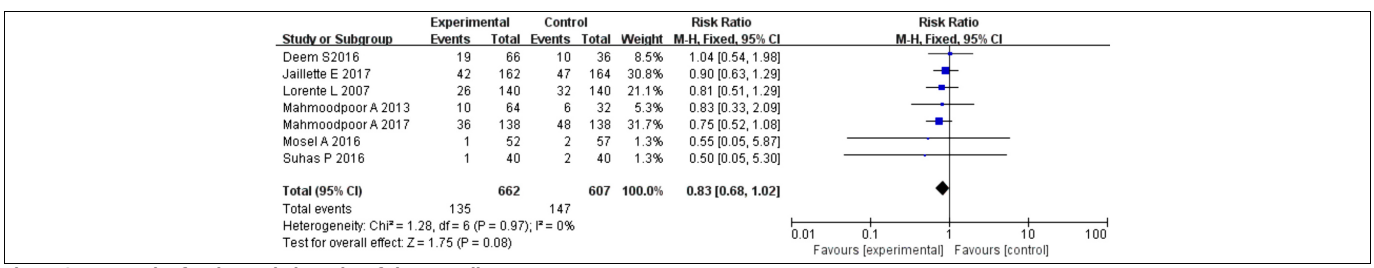

Figure 8: Forest plot for the pooled results of the mortality.

Two studies did not report ICU mortality, and the remaining seven studies reported ICU mortality.[28,30] The data of 662 patients in the experimental group and 607 patients in the control group were available to compare ICU mortality. No statistically significant difference was observed (RR = 0.83, 95% CI 0.68–1.02, p = 0.08, Figure 8).

The statistical results of the duration of mechanical ventilation, length of stay at ICU and hospital are summarised in Table II. Data consolidation was not done due to inconsistent statistical methods of continuous data. Only one study reported a statistical difference in the length of stay at ICU between the two groups.[32] The remaining studies reported no statistical difference in the duration of mechanical ventilation and the length of stay at ICU and hospital.

DISCUSSION

The results of the combined data showed that cuff modification could decrease the incidence of VAP. The heterogeneity test result was I^2 = 55%, p-value was 0.02. The reasons for this finding are primarily two-fold. On one hand, the experimental group had a larger sample size as compared to the control group (1134 patients in the experimental group and 803 patients in the control group). On the other hand, four of the nine RCTS used subglottic secretion drainage (SSD) in the experiment. The number of patients using SSD accounted for 33% of the total number in the experimental group. SSD has been confirmed to be an effective measure to prevent VAP.[33] As a result, a subgroup analysis was performed based on the various cuff design types, which revealed that compared with the conventional cuff, conical cuff, PU cuff, and PU-conical cuff had no advantage in reducing the incidence of VAP. However, the modified cuff with SSD could reduce the incidence of VAP compared with the conventional cuff.

Cuff modification is to increase the cuff's fit against the tracheal wall and decrease secretion leakage above the cuff, thus reducing the incidence of VAP. This meta-analysis showed that compared to the conventional cuff, the conical cuff, PU cuff and PU-conical cuff, did not reduce the incidence of VAP. However, studies *in vitro* found that modified cuff reduced the leakage around the tracheal cuff. The previous opinion indicated that cuff modification is inadequate for VAP prevention. This study confirmed the opinion with an accurate data. Similarly, the results of a recent large-scale cohort study of 15,388 cases indicated that the conical cuff was ineffective in preventing VAP.[34]

There are some possible reasons for these findings. One potential explanation may be that there are still defects in cuff modification. The conical cuff reduces the contact area between the cuff and the tracheal wall,[19] and it can reduce the formation of folds. This small contact area might lead to cuff slippage, which cannot effectively prevent the secretion from moving down. PU is one-tenth the thickness of PVC,[18] which consequently reduces the formation of channels between the tracheal wall and the cuff. However, because of the chemical and physical properties of PU, this material generates condensation, resulting in the presence of water in the cuff, which would affect the airtightness of the cuff after inflation and the accurate cuff pressure measurement.[35,36] Another potential reason may be that several clinical factors affect the airtightness of the cuff, including the cuff pressure, positive end-expiratory pressure, peak inspiratory pressure and even the mode of ventilation,[37,38] which are volatile in a clinical practice. A meta-analysis indicated that continuous cuff pressure monitoring could reduce the incidence of VAP,[39] but this was not performed in the included studies. Finally, it may be associated with the complicated pathogenesis of VAP. Critically-ill patients have various risk factors associated with VAP, including the patient's actual state, diagnosis and treatment-related operations, and drug-related factors,[40] which are not caused by a single element. Further, biofilm formation around the tracheal tube contributes to the development of VAP.[41,42]

Another subgroup analysis in this study showed that cuff modification combined with SSD could effectively reduce the incidence of VAP. Although cuff modification could reduce the leakage of secretions, secretions would still accumulate above the cuff and cannot be removed by oral aspiration, possibly leading to bacterial colonisation. SSD could promptly clear the secretions accumulated above the cuff. This study indicates that the timely removal of secretions accumulating above the cuff is an important approach for preventing VAP occurrence. A latest meta-analysis on SSD has shown that SSD can reduce the incidence of VAP and mortality of ICU.[43] Further research is necessary to explore whether a difference exists in reducing VAP incidence between the modified cuff and traditional cuff combined with SSD.

Another low-volume, low-pressure cuff was identified during the research but the studies were not included in the analysis. Several strategies are incorporated into the composite system in order to prevent oropharyngeal secretions from being aspirated. The strategies include the use of low-volume, low-pressure cuff, a securing flange, a tracheal seal monitor, multiple SSD ports, and a coated tube lumen.[44] Two RCTs confirmed that the composite system effectively prevented VAP occurrence in patients undergoing cardiac surgery.[45,46] Because the composite system combines multiple VAP prevention strategies, it is not easy to judge the role of the low-volume, low-pressure cuff; hence these two RCTs were not included in this study.

This study has some strengths. First, it included a large number of trials and patients in the analysis. Secondly, this study conducted subgroup analyses for different types of cuff modifications. In the systematic review conducted by Huang *et al*. on the tapered cuff, two studies used PU-conical cuff combined with SSD, which reduced the credibility of the

results on a tapered cuff. Third, through the sequential subgroup analysis of this study, it can be observed that the timely removal of secretions accumulated above the cuff is the key measure to prevent VAP occurrence.

However, there are also several limitations in this meta-analysis. First, although this study conducted a detailed subgroup analysis according to the design type of the cuff, the sample size of the subgroup analysis was too small, especially of the PU-conical cuff, which was used in only two studies. If further trials are conducted with large sample sizes, the results may not support this study. Second, a considerable heterogeneity exists among the included trials. The targeted population showed significant variations. There were differences in the definition of VAP, cluster prevention measures for VAP, and the study designs. Therefore, these factors may cause heterogeneity and have a potential impact on results of this study.

CONCLUSION

This study examined the impact of changing the endotracheal tube cuff on the prevention of VAP. It was observed that improvements of the cuff could reduce the incidence of VAP. The modified cuff would reduce the leakage of subglottic secretions, and the SSD would timely remove the secretions accumulated above the cuff. It is recommended to use the modified cuff combined with SSD endotracheal tube.

COMPETING INTEREST:
All authors declared no competing interests.

AUTHORS' CONTRIBUTION:
YL, CZ, HZ: Contributed to the conception and design of the study.
JB, MS: Contributed to acquisition, analysis, and interpretation of the data.
YW: Contributed to draft the manuscript.
All authors have approved the final version of the manuscript to be published.

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