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Prevention of ventilator-associated pneumonia by metal-coated endotracheal tubes: a meta-analysis

Yuxin Yang^{1†}, Xuan Xiong^{2†}, Xiaofei Wang³, Qionglan Dong^{1*} and Lingai Pan^{4*}

Abstract

Purpose This study aimed to evaluate whether endotracheal tubes (ETTs) with a metal coating reduce the incidence of ventilator-associated pneumonia (VAP) compared to uncoated ETTs.

Methods An extensive literature review was conducted to find studies that compared metal-coated ETT with uncoated ETT across four databases: PubMed, Embase, Cochrane Library, and Web of Science. The search parameters were set from the inception of each database until June 2024. The primary outcome measures were the rates of VAP and hospital mortality. Two independent researchers carried out the literature selection, data extraction, and quality evaluation. Data analysis was performed with RevMan 5.4.1. Furthermore, a Deeks funnel plot was used to evaluate potential publication bias in the studies included.

Results Following the screening process, five randomized controlled trials (RCTs) encompassing a total of 2157 patients were identified. In terms of the primary outcome, the VAP incidence was found to be lower in the group utilizing metal-coated ETT compared to those with uncoated ETT, demonstrating a statistically significant difference [RR=0.71, 95% CI (0.54–0.95), $P=0.02$]. No notable difference in mortality rates was observed between the two groups [RR=1.05, 95% CI (0.86–1.27), $P=0.65$]. Concerning secondary outcomes, two studies were evaluated to compare the mechanical ventilation duration (RR=0.60, 95% CI (–0.52, 1.72), $P=0.29$, $I^2=97%$) and intensive care unit (ICU) stay for both patient groups (RR=0.47, 95% CI (–1.02, 1.95), $P=0.54$, $I^2=50%$). Due to the marked heterogeneity, a comparison of mechanical ventilation length between the two patient groups was not feasible. However, both studies suggested no significant difference in ventilation duration between patients using metal-coated ETT and those with uncoated ETT.

Conclusions Metal-coated ETT show a lower occurrence of VAP compared to the uncoated ETT. Nevertheless, they do not considerably decrease the length of mechanical ventilation, the duration of ICU admission, nor do they reduce hospital mortality rates.

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Keywords Ventilator-associated pneumonia, Metal-coated endotracheal tubes, Uncoated endotracheal tubes, Meta-analysis

Introduction

Ventilator-associated pneumonia (VAP) is a type of pneumonia that arises after the placement of an artificial airway through procedures like tracheotomy or tracheal intubation, alongside mechanical ventilation [1]. VAP is associated with elevated mortality rates and prolonged hospital stays for individuals receiving mechanical ventilation. Several factors, such as the length of mechanical ventilation, patient position in bed, enteral nutrition, instances of aspiration, history of antibiotic usage, and various comorbid conditions, may all play roles in the onset of VAP [2]. Importantly, the endotracheal tube (ETT) has been recognized as an independent risk factor. Approximately 25–56% of intubated patients may experience VAP, mainly due to the colonization of bacteria on the surface of the intubation, which may subsequently progress to biofilms [3, 4]. These mechanisms are crucial for both the initiation and recurrence of VAP. However, there is currently limited research and a lack of clear solutions to this problem. In light of this issue, there has been a growing focus in research on methods for antibacterial surface coating and modifications of ETTs.

Tracheal intubation tubes are generally made from flexible substances like polyvinyl chloride (PVC) or silicone, which are conducive to microbial colonization and biofilm development on their surfaces, subsequently heightening the risk of pneumonia [5]. In the last few years, significant improvements have been achieved in the design of ETT, with antibacterial coatings presenting promising alternatives to address the problem of microbial adherence on the surfaces of instruments [6]. Various strategies have been developed by researchers, including active techniques that directly eliminate microorganisms from the device surface, passive techniques that alter the surface's composition and textures to establish pollution-resistant surfaces, and hybrid approaches that give ETT both active antibacterial and passive antifouling characteristics.

Among a range of metals and metal nanoparticles (NPs) known for their antibacterial properties, silver, zinc, selenium, and titanium dioxide have been thoroughly investigated, especially as coatings for ETT. The secretions from patients who are undergoing endotracheal intubation, which may be contaminated, can infiltrate the lungs through two main routes: via the area surrounding the endotracheal tube (micro inhalation) and along the surface of the endotracheal tube (biofilm development due to microbial colonization) [7].

A variety of studies have shown that biofilm formation on endotracheal tubes is a major factor contributing to the occurrence of VAP in patients who are intubated [8–11]. In recent times, the emergence of antibacterial coating materials has provided promising options for addressing the problem of biofilm formation on medical device surfaces. Among these, silver has been the most thoroughly researched precious metal over the past three decades and is the only one that has completed numerous clinical trials leading to commercialization [12, 13]. Following its successful application in urinary catheters in 1990, research into its possible uses in endotracheal tubes began [14]. Silver aids in the binding of ions with components of bacterial cells, which results in modifications to several essential bacterial functions [15, 16]. These include increased permeability of the cell, membrane disruption, oxidative damage stemming from interrupted cellular respiration, and variations in protein function [6]. Numerous silver-based compounds, alloys, nanoparticles (NPs), and materials have been studied as antibacterial coatings for ETT, owing to their wide-ranging mechanisms of action. These substances can either be directly integrated into biomaterials for combined uses or created as silver nanomaterials. Hartmann et al. were pioneers showed that silver-plated ETT can effectively suppress the growth of *Pseudomonas aeruginosa* in a continuous ventilation pharyngeal lung model, achieving a reduction of twofold after 50 h of incubation [17]. Silver nanoparticles (AgNPs) have increasingly become a promising safety strategy, while included in ETT, they showed improved antibacterial effectiveness against bacteria, viruses, and fungi, thereby reduced the cytotoxicity typically linked to silver ion release [6, 18].

A novel ETT has been created, featuring a sub-micron coating of a noble metal alloy (NMA), which consists of gold, silver, and palladium, in addition to the standard silver-coated ETT. This coating adheres firmly to the tube's surface and does not significantly leach into the body (Bactiguard Infection Protection, BIP). The galvanic properties of noble metal alloys produce a microcurrent that helps to minimize the formation of bacterial biofilm, thus reduce the colonization of the ETT and lowering the risk of respiratory infections [19].

While ETT that are coated with metals may decrease microbial growth on their surfaces [17, 19, 20], their impact on the rates of VAP and mortality

during hospital stays remains unclear in comparison to uncoated ETT. To investigate a more detailed understanding of the differences in VAP incidence between metal-coated and uncoated ETT, we performed a meta-analysis of randomized trials.

Materials and methods

Data sources

A combination of electronic and manual retrieval methods was employed to carry out literature searches and initial screenings across four different databases: PubMed, Embase, Cochrane Library, and Web of Science. The search was limited to publications from the inception of each database until June 2024. Our search strategy incorporated terms from titles, abstracts, and keywords, including “Ventilator Associated Pneumonia” or “VAP” AND (“noble metal coating of endotracheal tubes” or “noble metal alloy coated endotracheal tubes” or “NMA coated ETTs” or “silver coated endotracheal tubes” or “internally coated endotracheal tubes” or “coated endotracheal tubes” or “selenium nanoparticle coatings” or “ZnO nanoparticles” or “titanium” or “aluminum dioxide coated endotracheal tubes”). The search was limited to studies involving humans and published in English. Additionally, the reference lists of relevant studies were scrutinized to identify further pertinent literature.

Study inclusion criteria and outcome measurements

Inclusion criteria: (1) Patients who were 18 years or older, (2) Patients were received intubation with either metal-coated or non-coated endotracheal tubes, and expected to have a ventilation duration exceeding 24 h, (3) RCTs published in English. (4) Definition of VAP: the duration of mechanical ventilation or tracheal intubation must be between 24 and 72 h, accompanied by new evidence of pulmonary infection.

Exclusion criteria: (1) Studies involved non-human subjects, (2) Studies that were non-comparative, (3) Studies which were lack of extractable data, and (4) Studies that were not original research.

Outcome measurements: Primary outcome: (1) Incidence of VAP, (2) Hospital mortality rate. Secondary outcome: (1) Mechanical ventilation time, (2) the length of the ICU-stay. Subgroup analysis: metal-coated ETT could be categorized into noble metal-coated ETT and silver-coated ETT, which could be compared to uncoated ETT.

Literature screening and data extraction

A literature search was carried out by two researchers, with any discrepancies resolved through discussions with a third researcher. In cases where more comprehensive data is needed, the corresponding author should be contacted to obtain access. From the initial

literature screening, pertinent details were gathered, including patient demographics (such as age) and literature-related aspects (like publication date, authorship, and country). The collected literatures were evaluated according to the specified inclusion and exclusion criteria. Any absent data would be relayed to the author by email to finalize the characterization study. If the author failed to reply or if the information provided was still ambiguous, the corresponding field would be indicated as ‘not reported (NR)’.

Literature quality evaluation

Two researchers evaluated the literature’s quality independently by utilizing the Cochrane risk of bias tool. The assessment of bias risk was carried out following the criteria specified in the Cochrane Handbook 5.1.0, which encompassed reviews of random sequence generation, allocation concealment, the blinding of both participants and those providing interventions, the blinding of outcome assessors, the completeness of outcome data, selective reporting of findings, and various other potential bias sources. According to the risk assessment criteria, each aspect was classified as ‘low risk of bias,’ ‘unclear,’ or ‘high risk of bias’ [21].

Statistical analysis

The analysis of data was performed employing Revman 5.4.1 software. This study’s outcome measures comprised both dichotomous and continuous variable data. The assessment of dichotomous utilized the hazard ratio (RR) along with its 95% confidence interval (95% CI) as measures of effect. Continuous variables were evaluated through the mean difference (MD) and its related 95% CI. For continuous data presented as median and interquartile range in research reports, the methodology formulated by Luo et al. [22] was applied to calculate the mean and standard deviation from the median and interquartile range. The significance threshold was established at $P=0.05$, and the I^2 test was employed to assess the degree of heterogeneity in each study. If significant heterogeneity was not present ($I^2 < 50\%$ and $P \geq 0.05$), we used fixed effects models to pool outcomes; we used random effects models when significant heterogeneity was present ($I^2 \geq 50\%$ or $P < 0.05$). In instances where heterogeneity was identified, a sensitivity analysis was carried out utilizing a one-by-one exclusion approach to determine whether excluding individual studies would affect the overall findings. Moreover, a funnel plot was generated to assess publication bias amongst the included studies.

Results

We identified 103 articles from the electronic database, PubMed (34), Embase (43), Cochrane Library (16), and Web of Science (10). After removing duplicates and performing an initial examination, 9 articles were chosen. A subsequent review and comprehensive analysis of the full texts led to the final selection of 5 articles for meta-analysis, which encompassed 2157 patients altogether. The literature screening process was illustrated in Fig. 1, while the basic characteristics of the included studies were presented in Table 1 (Supplementary Information, Table S1). The quality assessment of the literature was performed using the Cochrane bias risk tool, which evaluated the reliability of the five studies included. The

results suggested that the overall quality of the literature was dependable (Fig. 2).

Meta analysis results

Primary outcome

VAP incidence: Four studies [12, 13, 23, 24] were included, comprising a total of 2036 patients: 1036 patients in the group using metal-coated ETT and 1000 patients in the group using uncoated ETT. Compared to the uncoated ETT group, the metal-coated ETT group demonstrated a statistically significant reduction in the incidence of VAP [RR=0.71, 95% CI (0.54, 0.95), $P=0.02$]. There was no significant heterogeneity among the studies (Fixed, $I^2=41%$, $P=0.16$) (Fig. 3). Figure 5A

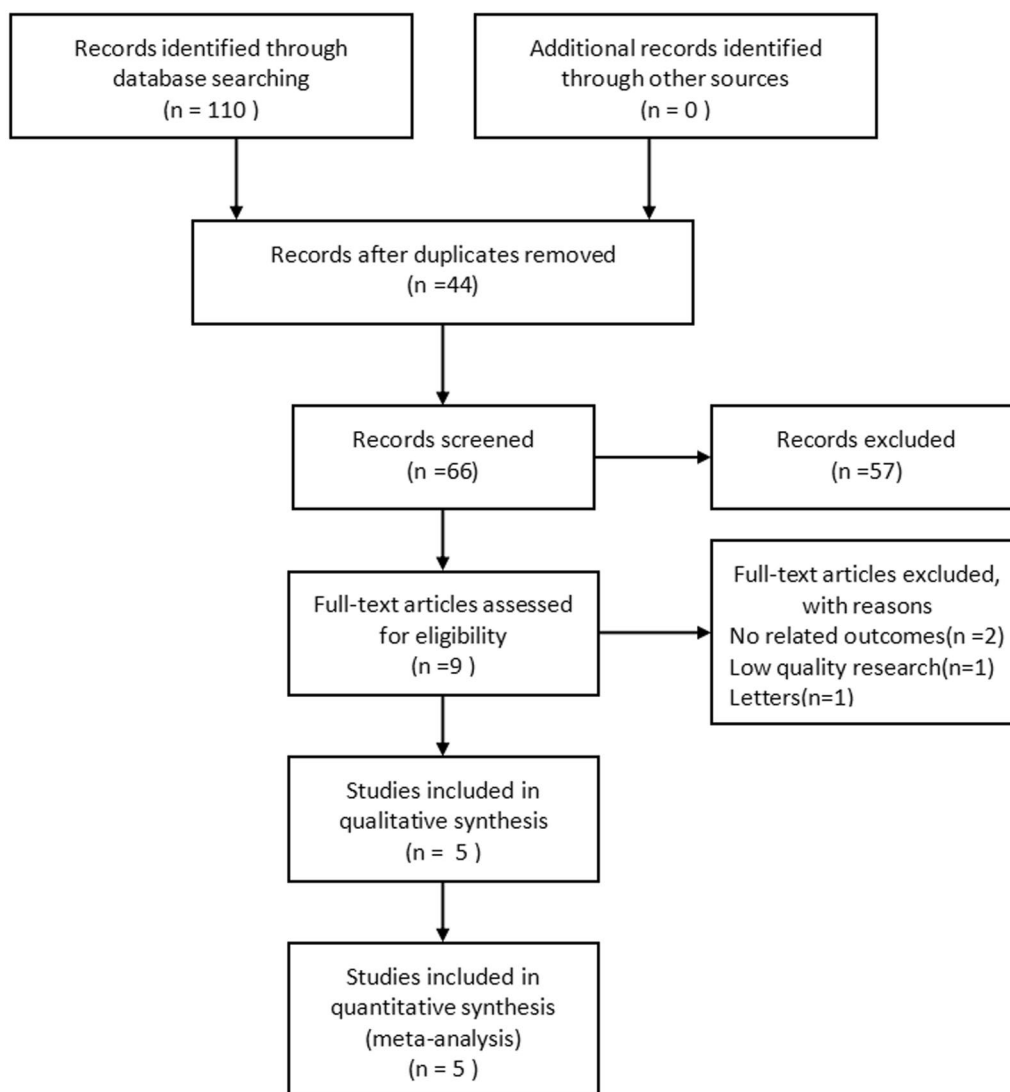


Fig. 1 Flow chart of literature screening for Meta-analysis on the Prevention of ventilator-associated pneumonia by metal-coated endotracheal tubes

Table 1 The main characteristics of the studies included in the meta-analysis (Supplementary Information (Details of the design of all studies))

References	Age (Metal coated ETT* vs. Control, years)	Gender (female ratio)	Population	Severity of illness (Metal coated ETT vs. Control, years)	ETT trial		Analyzed population	Outcomes	Adverse events
					Metal coated ETT	Control			
Pierre Damas [23]	67.9 (56.4–74.7) versus 67.3 (58–74.5)	75 (44.6) (44.5) versus 69	Patients required mechanical ventilation for 24 h and were 18 years old	SOFA Scores 8 (6–10) versus 8 (6–11)	Noble metal-coated ETT	Uncoated ETT	323 (168 vs 155)	VAP* incidence, Antibiotic consumption, Bacterial colonization, length of the ICU-stay, ventilatory days, hospital mortality	NR
Behnam Mahmodiyeh [24]	42.93(± 1.42) vs47.86 (±2.08)	10(17.55) vs15(26.32)	The intubated patients age 18 to 60 years, GCS ≤ 10	NR*	Noble metal-coated ETT	Supraglottic suctioning ETT	114 (57 vs 57)	VAP incidence, Frequency of positive culture	NR
Ata Mahmood-poor [12]	59 (43–69)vs61 (44–69)	15(33.33) vs15(33.33)	Patients aged 18 to 80 years who required mechanical ventilation for > 48 h	APACHE II scores 22(19–26)vs 21 (20–24)	Silver-coated ETT	Uncoated ETT	90(45vs45)	VAP incidence, length of the ICU-stay, ventilatory days, hospital mortality	NR
Marin H. Kollif [13]	60.9 (± 15.7)vs 62.0 (± 15.4)	309(40.3) vs327(44)	Adults ≥ 18 years old and mechanical ventilation with an endotracheal tube for 24 h or longer	APACHE II scores 21.4 (±7.4)vs 21.6 (±7.5)	Silver-coated ETT	Uncoated ETT	1509(766vs743)	VAP incidence, time to occurrence of VAP, hospital mortality	respiratory disorders, gastrointestinal tract disorders, Device malfunction
Jordi Rello [25]	66.5(± 14.0) vs62.6(± 16.2)	21(34.42) vs19(31.67)	Patients required mechanical ventilation for 24 h and were 18 years old	APACHE II scores 21.0(±6.7)vs 21.2(±7.6)	Silver-coated ETT	Uncoated ETT	121(61vs60)	Tube colonization and bacterial burden, Modified CPIS (30), hospital mortality	Dysphagia, laryngospasm, glottis edema, residual Silver concentrations

*ETT, endotracheal tubes; VAP, ventilator-associated pneumonia; NR, no report

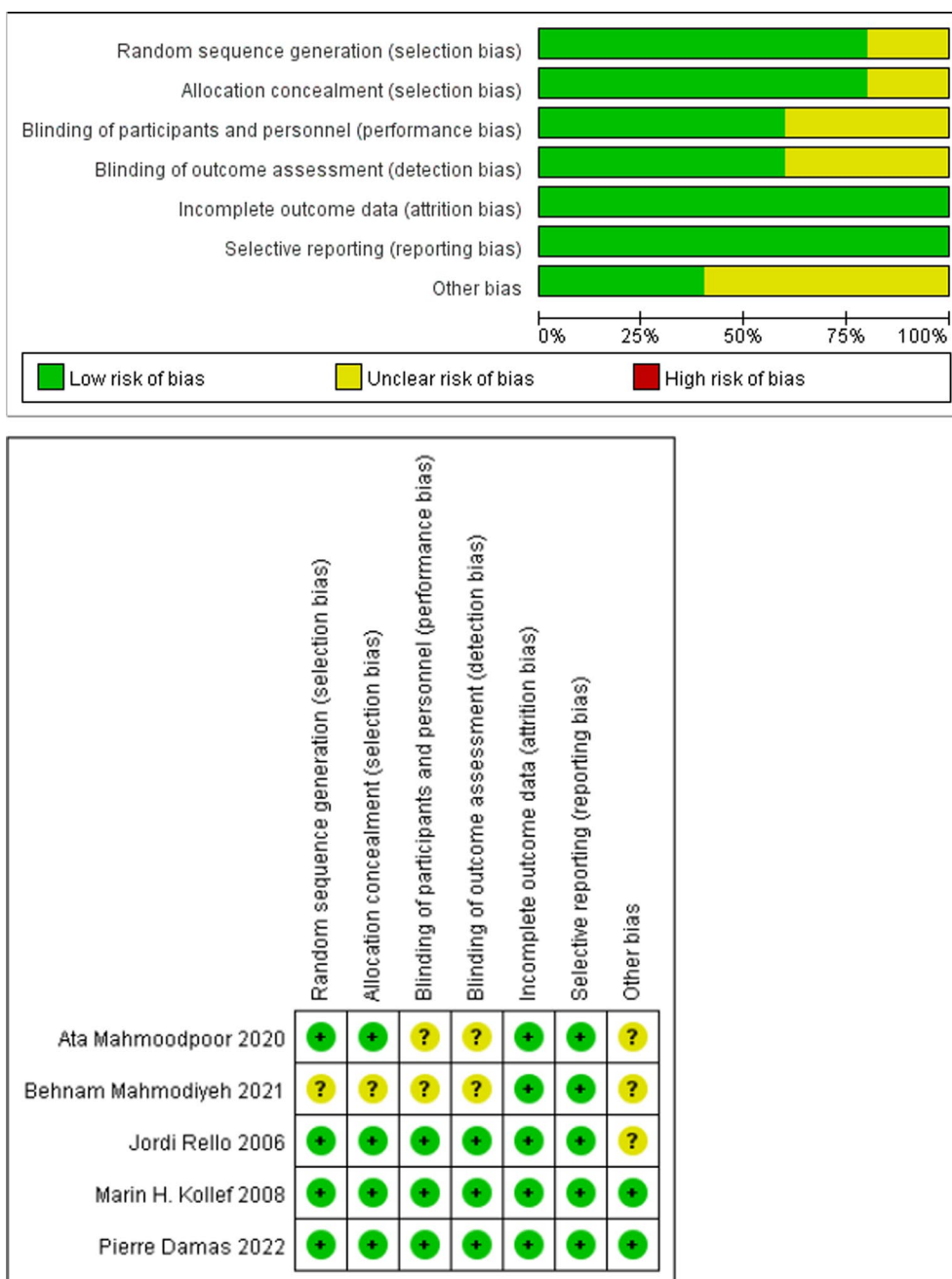


Fig. 2 Bias risk assessment results of literatures in the Meta-analysis

illustrates the publication bias and sensitivity analysis of VAP incidence between metal-coated ETT and uncoated ETT.

Hospital mortality rate: Three studies [12, 23, 25] were included in the analysis, encompassing a total of 534 patients: 274 patients utilized metal-coated ETT, while 260 patients used uncoated ETT. The analysis

revealed no significant difference in hospital mortality rates between the metal-coated and uncoated ETT groups [RR = 1.05, 95% CI (0.86, 1.27), $P=0.65$]. Additionally, there was no significant heterogeneity among the studies (Fixed, $I^2=0%$, $P=0.37$) (Fig. 4). Figure 5B presents the publication bias and sensitivity analysis of hospital mortality between metal-coated ETT and uncoated ETT.

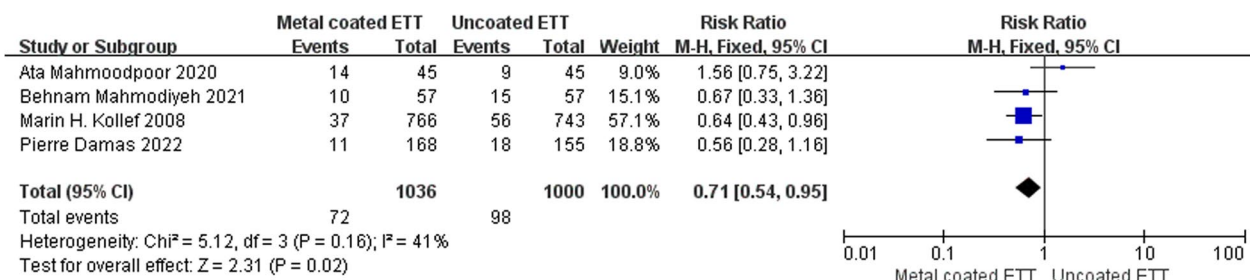


Fig. 3 Comparison of VAP incidence between Metal coated ETT and Uncoated ETT

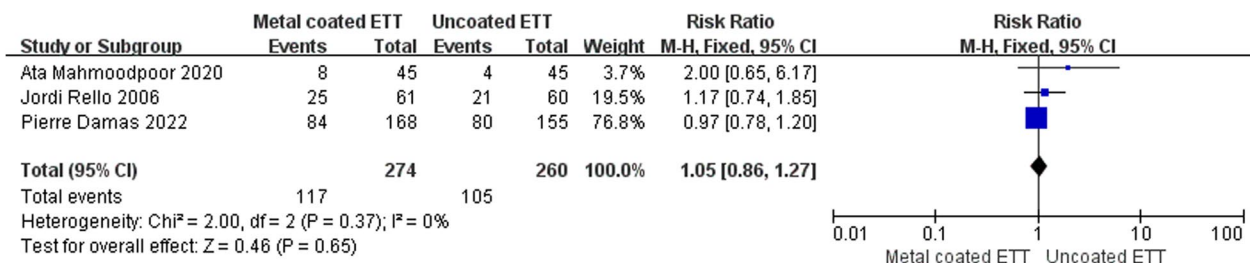


Fig. 4 Comparison of hospital mortality between Metal coated ETT and Uncoated ETT

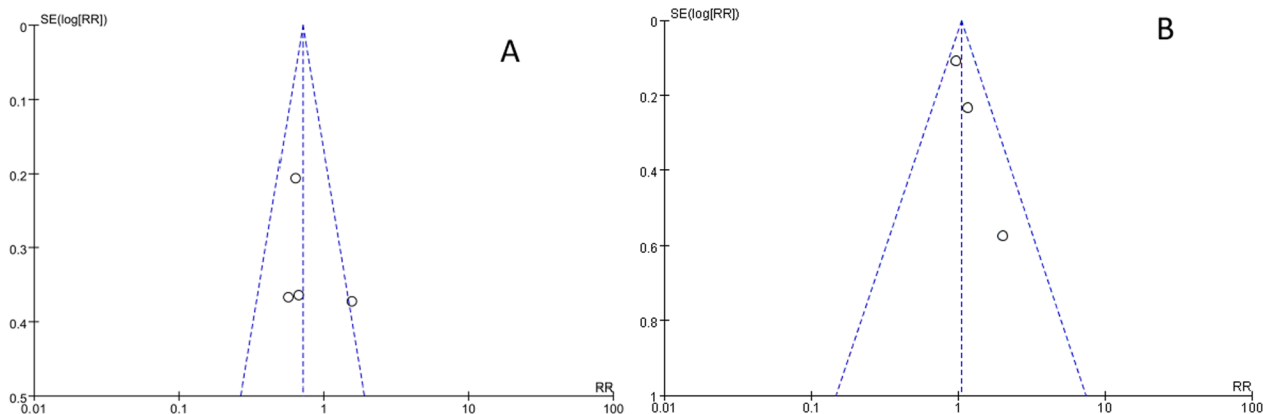


Fig. 5 Publication bias and sensitivity analysis of the main outcome. A, VAP incidence between Metal coated ETT and Uncoated ETT. B, hospital mortality between Metal coated ETT and Uncoated ETT

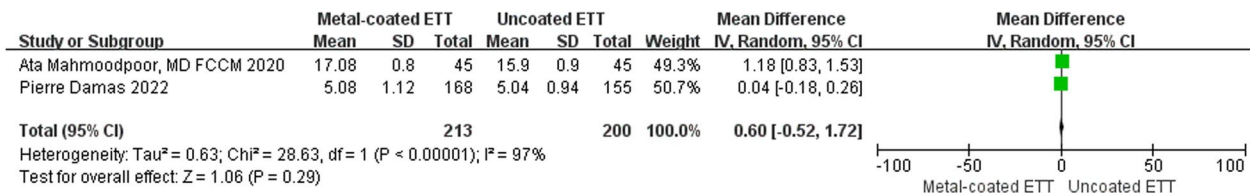


Fig. 6 Comparison of mechanical ventilation time between Metal coated ETT and Uncoated ETT

Secondary outcome

Mechanical ventilation time: Two studies [12, 23] were included, comprising a total of 413 patients: 213

patients utilized metal-coated ETT, while 200 patients used uncoated ETT. Random effects models indicated no significant difference (RR = 0.60, 95% CI (-0.52,

1.72), $P=0.29$). However, there was significant heterogeneity between the two studies (Random, $I^2=97%$, $P<0.00001$) (Fig. 6).

The length of the ICU-stay: Two studies [12, 23] were included, comprising a total of 413 patients: 213 patients in the group using metal-coated ETT and 200 patients in the group using uncoated ETT. There was no significant difference in ICU hospitalization time between the two patient groups (RR=0.47, 95% CI (-1.02, 1.95), $P=0.54$). There was significant heterogeneity among the studies (Random, $I^2=50%$, $P=0.16$) (Fig. 7).

Subgroup analysis

Noble metal-coated ETT versus uncoated ETT

Two studies [23, 24] were included, encompassing a total of 437 patients: 225 patients in the group using noble metal-coated ETT and 212 patients in the group using uncoated ETT. When comparing the uncoated ETT group, the incidence of VAP was lower in the noble metal-coated ETT group; however, this difference was not statistically significant (RR=0.61, 95%

CI (0.37–1.01), $P=0.06$), and there was no significant heterogeneity between the two studies (Fixed, $I^2=0%$, $P=0.74$) (Fig. 8).

Silver-coated ETT versus uncoated ETT

Two studies [12, 13] were included, encompassing a total of 1599 patients: 811 patients in the silver-coated ETT group and 788 patients in the uncoated ETT group. The analysis revealed no significant difference in the incidence of VAP between the two groups [RR=0.95, 95% CI (0.40–2.25), $P=0.90$]. However, there was significant heterogeneity between the two studies (Random, $I^2=77%$, $P=0.04$) (Fig. 9).

Discussion

This research assessed the effects of metal-coated ETT in contrast to uncoated ETT on the occurrence of VAP among patients who were intubated for more than 24 h. The findings showed that the use of metal-coated ETT could notably decrease the rate of VAP when compared to their uncoated counterparts. However, there was no significant variation in hospital mortality rates between the two cohorts. Furthermore, a comparison of the

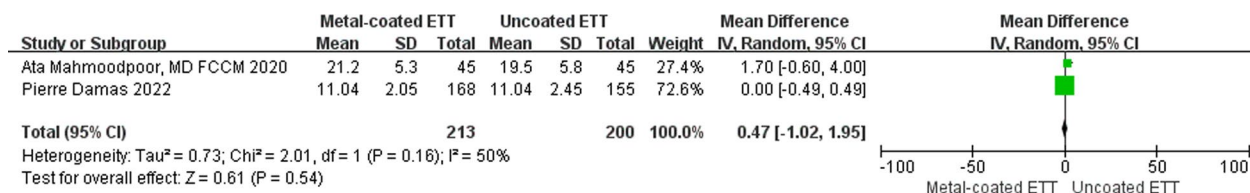


Fig. 7 Comparison of length of the ICU-stay between Metal coated ETT and Uncoated ETT

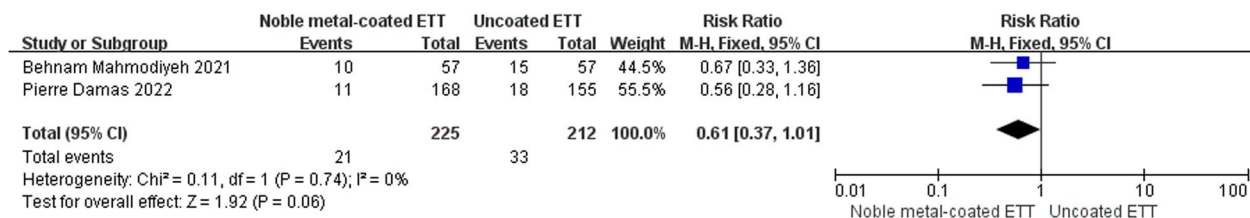


Fig. 8 Comparison of VAP incidence between Noble metal-coated ETT and Uncoated ETT

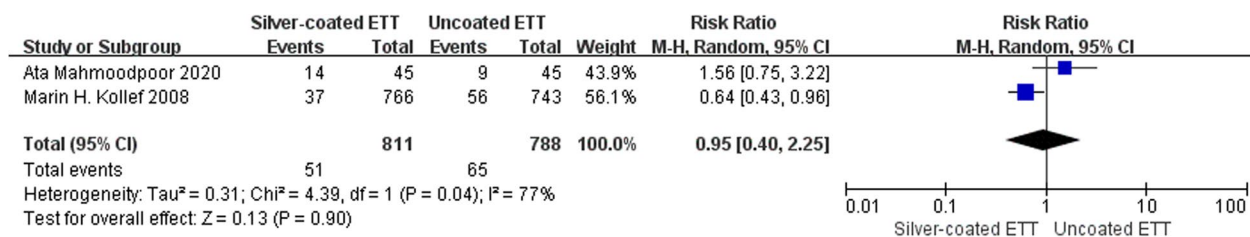


Fig. 9 Comparison of VAP incidence between Silver-coated ETT and Uncoated ETT

duration of mechanical ventilation and length of stay in the ICU between the two patient groups demonstrated considerable variability in the studies included. Despite this, both initial studies indicated no statistically significant differences in mechanical ventilation duration and length of ICU stay between the groups using metal-coated ETT and those with uncoated ETT.

Earlier studies conducted *in vitro* and in clinical practice have demonstrated that ETT coated with silver can diminish bacterial colonization and biofilm development [26, 27]. The studies we analyzed also indicated that at equivalent thresholds (++, +++, or $\geq 10^4$ colony-forming units/mL), silver-coated ETT were linked to a postponement in implantation ($P=0.02$, log-rank test; $P=0.10$, Wilcoxon's test) when compared to the control group. Furthermore, this association corresponded with a decrease in the peak bacterial load from tracheal inhalations over a span of 7 days (mean log-transformed burden: 4.2 ± 2.3 vs. 5.5 ± 1.7 log colony-forming units/mL; $P=0.02$, Wilcoxon's test). We reviewed three randomized controlled trials (RCTs) that contrasted silver-coated ETT with uncoated ETT. Among these, two trials evaluated the occurrence of VAP as the main endpoint. Our subgroup analysis showed no noteworthy difference in the incidence of VAP between the groups using silver-coated and uncoated ETT. However, the studies exhibited heterogeneity, and the study by Ata Mahmoodpoor [12] had a small sample size, which may have influenced these findings. In contrast, a multicenter RCT conducted by Marin H. Kollef et al. involved 1509 patients with tracheal intubation lasting more than 24 h demonstrated that, in multivariate logistic regression analyses, the treatment group was associated with a reduced risk of developing VAP at any time (odds ratio for silver-coated vs. uncoated, 0.52; 95% CI 0.33–0.82 [$P=0.005$]) and within 10 days of intubation (odds ratio, 0.44; 95% CI 0.26–0.73 [$P=0.001$]). Additionally, Cox regression analysis indicated that the treatment group was associated with a delayed time to the occurrence of VAP (hazard ratio, 0.55; 95% CI 0.37–0.84 [$P=0.006$]).

Prior research has shown that BIP ETT (Bactiguard® coated ETTs) are tolerated well and demonstrated favorable clinical outcomes during short-term intubation [28]. Our review focused on two studies [23, 24] encompassing a total of 437 patients. When comparing the noble metal-coated ETT group to those using uncoated ETT, a lower rate of VAP was observed, although this finding lacked statistical significance. It is important to note the heterogeneity present between the two studies. Additionally, the investigation conducted by Behnam Mahmodiyeh et al. revealed that VAP symptoms manifested significantly sooner in patients who were intubated with

uncoated ETT than in those with a noble metal-coated ETT (5 ± 1.8 days vs. 8.5 ± 2.1 days, $P=0.001$).

Our detailed examination reveals that ETT with a metal coating can markedly lower the occurrence of VAP when compared to ETT without coating; nonetheless, there is no notable difference in mortality rates during hospitalization. We believe this result can be linked to the various factors contributing to mortality in patients on mechanical ventilation, where VAP represents merely one of the several influences, and the overall reported rate of VAP in this study is relatively minimal. Despite the correlation between VAP and extended periods of mechanical ventilation as well as longer ICU admissions, the research we reviewed consistently indicated no significant variances in either the duration of mechanical ventilation or the length of ICU stays for patients using coated versus uncoated ETT [12, 23]. We argue that the adoption of further strategies aimed at preventing VAP is crucial for minimizing extended mechanical ventilation and reducing ICU lengths of stay. Traditional ICU studies have focused on “ventilator-free days” as a more effective marker than “intubation time.” However, since all the studies included in our analysis reported results based on intubation time and the length of ICU stays, it may be more beneficial to utilize “ventilator-free days” as the outcome measure in future studies on VAP.

Nonetheless, promoting metal-coated ETT necessitates caution due to ongoing debates about its safety. In investigations of AgNPs, after 28 days of oral exposure in domestic rabbits, these nanoparticles were found in the basal layer, macrophages, and the connective tissue of the submucosal layer [29]. Furthermore, studies suggest that when AgNPs of various sizes were administered intravenously to rats, there was a redistribution of these nanoparticles to the liver, lungs, heart, and other organs, highlighting their systemic distribution [30]. Although the safety of silver-coated ETT has been reported by Marin H. Kollef [13] and Jordi Rello [25], they did not explore if residual silver ions persist in the body or if additional harm might be inflicted. Silver-coated ETT have been on the market since 2013, with claims from the manufacturer that this coating did not release silver ions into the surrounding environment. Nonetheless, there is still a lack of clinical studies that substantiate its safety. Besides silver-coated ETT, other variations include those coated with zinc oxide nanoparticles (ZnO NPs) [31], selenium nanoparticles (SeNPs) [32], and titanium dioxide nanoparticles (TiO₂ NPs) [33]. However, no research currently exists that examines the preventive effects of these metal-coated ETTs on VAP, and their safety requires additional scrutiny.

Traditional methods for preventing VAP include preventing pulmonary aspiration of oropharyngeal

secretions, draining subglottic secretions with specially designed devices, measuring gastric residual volume, and performing regular oropharyngeal care with chlorhexidine, among others [34, 35]. In recent years, the use of inhaled antibiotics to prevent VAP in critically ill patients has garnered significant attention from medical professionals. A high-quality study found that VAP developed in 62 patients (15%) in the inhaled amikacin group and in 95 patients (22%) in the placebo group at 28 days, resulting in a difference in restricted mean survival time to VAP of 1.5 days (95% CI 0.6–2.5; $P=0.004$) [36]. However, considerable uncertainty remains regarding the selection of appropriate antibiotics for different patients and the optimal duration of inhalation. Additionally, the choice of nebulizer and filter within the respiratory circuit is also very important. Although our research findings indicate that metal-coated ETT can reduce the incidence of VAP compared to uncoated ETT [RR=0.71, 95% CI (0.54–0.95), $P=0.02$], there is currently no relevant research comparing the effectiveness of inhaled antibiotics and metal-coated ETT in preventing VAP, which suggests that we can conduct relevant research in the future.

This research has a few limitations. The studies assessed in our review were few in number, and a number of them had smaller sample sizes, which could lead to a small study effect. Furthermore, the criteria for inclusion and exclusion differed across various studies, which might elevate the heterogeneity of our findings. Lastly, variations in VAP prevention measures, aside from endotracheal tube management, may influence the incidence rates of VAP across different research centers.

Conclusion

Compared to uncoated ETT, metal-coated ETT can reduce the incidence of VAP. However, they do not shorten the duration of mechanical ventilation or the length of stay in the ICU, nor improve hospital mortality. The widespread clinical application of metal-coated ETT requires careful consideration of their safety and economic viability, and further studies need to be conducted to confirm their safety and effectiveness.

Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1186/s13054-024-05095-8>.

Additional file 1.

Author contributions

LP contributed to the conception; YY and XX: acquisition, analysis, interpretation of data, and drafting for the work; XW and QD: participate in literature screening; LP: reviewing the work critically for important intellectual content. All authors have final approval of the version to be published and have agreed

to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Availability of data and materials

No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate

Ethics approval and consent to participate does not apply.

Consent for publication

Consent for publication does not apply.

Competing interests

The authors declare no competing interests.

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