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Research article

# Role of bronchoscopy in the management of patients with suspected or suffering from ventilator-associated pneumonia: A meta-analysis

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ABSTRACT

*Background:* The utility of bronchoscopy in the treatment of patients with ventilator-associated pneumonia (VAP) has been proposed, although prior research has yielded inconclusive findings. This systematic review and meta-analysis were conducted to examine the impact of bronchoscopy on mortality rates, duration of mechanical ventilation (MV), and length of stay in the intensive care unit (ICU) among patients with VAP.

*Methods:* Relevant randomized controlled trials (RCTs) and cohort studies were acquired by conducting a comprehensive search in the PubMed, Embase, and Cochrane Library databases. To account for the potential heterogeneity, a random-effects model was utilized to combine the findings and incorporate its potential influence.

*Results:* Eight RCTs and three cohort studies, including 3907 patients with highly suspected or clinically diagnosed VAP, were included. Compared to the controls, bronchoscopy use was not associated with a significant effect on all-cause mortality (relative risk [RR]: 0.81, 95 % confidence interval [CI]: 0.62 to 1.05, $p = 0.12$; $I^2 = 57$ %). Subgroup analysis showed that bronchoscopy used for the microbiological diagnosis of VAP was not associated with reduced mortality (RR: 0.92, 95 % CI: 0.75 to 1.13), while therapeutic bronchoscopy use was associated with significantly reduced mortality (RR: 0.53, 95 % CI: 0.35 to 0.81). The duration of MV or length of ICU stay was not significantly different between groups.

*Conclusions:* Bronchoscopy use for the purpose of the microbiological diagnosis of VAP did not reduce short-term mortality compared to diagnosis without bronchoscopy use, while therapeutic bronchoscopy use was associated with reduced mortality in these patients.

## 1. Introduction

Ventilator-associated pneumonia (VAP) is a form of hospital-acquired pneumonia occurring in patients who have been on mechanical ventilation (MV) for at least 48 h [1,2]. It is a common infection among ventilated patients, with rates varying from 5 % to 40 % depending on clinical factors [3]. VAP increases the mortality rate, lengthens the intensive care unit (ICU) stay, and raises the

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healthcare costs of patients [4,5]. Risk factors include age, comorbidities, immunocompromised status, respiratory weakness, and male gender [4,6]. Treatment options for VAP are currently limited despite its severe consequences [7].

Bronchoscopy is a widely utilized procedure that effectively eliminates contaminants and foreign substances from the respiratory tract while also facilitating the acquisition of pulmonary tissue samples for diagnostic purposes [8]. The timely implementation of bronchoscopy within 24 h of intubation has been demonstrated to enhance the survival rates of individuals with aspiration pneumonia [9]. Furthermore, the combined utilization of bronchoscopy and bronchoalveolar lavage (BAL) enables the identification of causative pathogens in patients suffering from aspiration-induced lung injury, subsequently enabling the removal of persistent sputum from the airways in cases of refractory pulmonary infection [10,11]. Given the crucial role of microbiological diagnosis [12] and effective airway management [13] in the successful treatment of VAP, there has been a suggestion that the inclusion of bronchoscopy in VAP management could potentially benefit the prognosis of patients [10]. Consequently, the objective of this study was to conduct a comprehensive systematic review and meta-analysis to examine the impact of bronchoscopy utilization on mortality rates, duration of MV, and length of ICU stay among individuals diagnosed with VAP.

## 2. Materials and methods

During the design and implementation of this study, we followed the guidelines set out by PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) [14,15] and the Cochrane Handbook [16].

### 2.1. Study inclusion and exclusion criteria

This meta-analysis included studies that met the inclusion criteria specified by the PICOS principle:

P (patients): Studies involving patients on invasive MV and with clinically suspected or diagnosed VAP;

I (intervention): Studies that included a treatment (intervention) group involving the use of bronchoscopy. Generally, bronchoscopy is used for the microbiological diagnosis of VAP with bronchoalveolar lavage (BAL) to guide the antibiotic regimen, therapeutic purpose of fiberoptic bronchoscopy (FOB)-assisted sputum suction, or both;

C (control): Studies that included a control group without the use of bronchoscopy during treatment;

O (outcomes): Studies in which at least one of the following outcomes was reported: comparison of all-cause mortality during hospitalization between patients with and without the use of bronchoscopy, and differences in MV time or ICU stay between groups;

S (study design): Randomized controlled trials (RCTs) or cohort studies published as full-length articles in the English language.

Excluded from the analysis were studies that focused on patient populations other than those with VAP, studies that included patients undergoing noninvasive mechanical ventilation, single-arm studies lacking a control group of patients who did not receive bronchoscopy as part of their treatment, and studies that did not report the relevant outcomes of interest. We chose the study with the largest sample size for the meta-analysis when the patient populations overlapped between studies.

### 2.2. Literature search

The Medline (PubMed), Embase (Ovid), and CENTER (Cochrane Library) databases were searched using the following terms: (1) "bronchoscope" OR "bronchoscopic" OR "bronchoscopy"; (2) "ventilator" OR "ventilation"; and (3) "pneumonia" to identify relevant studies. Only studies that included human subjects and were published as full-length articles in peer-reviewed journals were considered. The detailed search strategy for each database and the exact number of retrieved articles are shown in Supplemental File 1. Additionally, references to related reviews and original articles were screened as part of the final database search. The final database search was conducted on September 10, 2023.

### 2.3. Data collection and quality evaluation

Two authors independently conducted the database searches, and performed the data collection, and quality assessment. In the event of disagreements, discussions were held with the corresponding author. The data collected encompassed various aspects, including overall study information (such as first author, publication year, and study country), study design (randomized controlled trials or cohort studies), patient information (diagnosis, number of patients, mean age, and sex), details of bronchoscopy utilization in treatment, control details, duration of follow-up, reported outcomes, and matched or adjusted variables. The quality of the included randomized controlled trials (RCTs) was assessed using the Cochrane Risk of Bias Tool [16]. This tool enables evaluating various aspects, such as random-sequence generation, allocation concealment, blinding of participants and outcome assessment, addressing incomplete outcome data, selective reporting, and addressing other sources of bias. For cohort studies, the Newcastle–Ottawa Scale (NOS) [17] was employed to score the studies based on the participant selection, comparability of groups, and validity of outcomes. The NOS scoring system consists of nine stars, with a higher number indicating higher quality.

### 2.4. Statistical analysis

The outcomes of the discontinuous variables were summarized as a risk ratio (RR) and the corresponding 95 % confidence interval (CI), while the outcomes of the continuous variables were presented as the mean difference (MD) and 95 % CI. The RR data and the corresponding standard error (SE) were computed using either the 95 % CI or $p$ value, and then subjected to logarithmic transformation

to stabilize the variance and normalize distribution [16]. Heterogeneity was assessed using the Cochrane Q test [16]. The $I^2$ statistic was also calculated, with $I^2 > 50$ % indicating significant heterogeneity [18]. A random-effects model was used to pool the results, because this model could incorporate the potential influence of heterogeneity [16]. Analysis of the predefined subgroups was conducted to evaluate the study characteristics on the outcomes, such as the study design (RCTs or cohort studies), details of bronchoscopy use (only for microbiological diagnosis or involving therapeutic use), and follow-up duration. An evaluation of the publication bias was conducted via a visual inspection using funnel plots and by performing Egger's regression asymmetry test [19]. In the analyses, $p < 0.05$ was considered statistically significant. Statistical analyses were conducted using RevMan (Version 5.1; Cochrane, Oxford, UK) and Stata software (version 12.0; Stata Corporation, College Station, TX, USA).

### 2.5. Certainty of the evidence

We used the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) working group methodology to assess the certainty of evidence across the domains with a risk of bias: consistency, directness, precision, outcome, and publication bias [20].

## 3. Results

### 3.1. Literature search

Fig. 1 depicts a flowchart outlining the process for the database search and study identification, which ultimately led to the selection of the studies for inclusion in the meta-analysis. Initially, a total of 635 articles were obtained through the database search, which was subsequently reduced to 487 after eliminating duplicate records. Subsequently, 466 articles were excluded based on an evaluation of their titles and abstracts, primarily due to their lack of relevance to the objective of the present meta-analysis. Following this screening process, 10 out of the remaining 21 articles underwent full-text reviews and were subsequently excluded for various

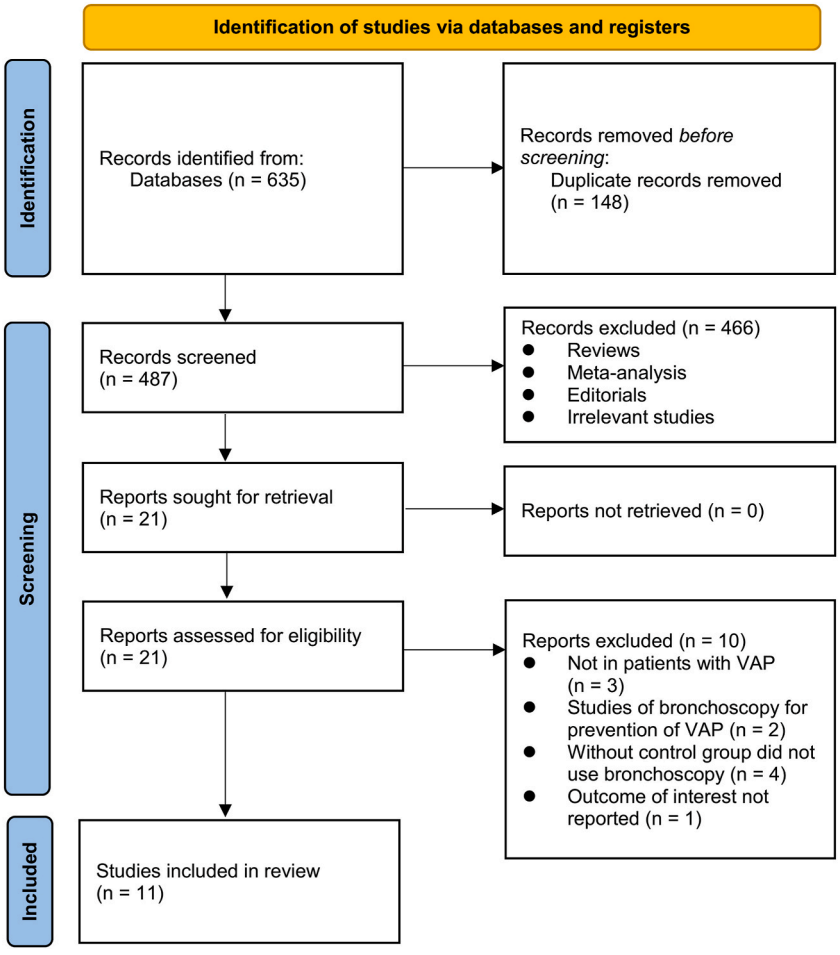


**Fig. 1.** Flowchart for the literature search and study inclusion.

**Table 1**
Characteristics of the included studies.

| Study | Country | Design | Diagnosis | Number of patients | Mean age (years) | Male (%) | Bronchoscopy group (n, details) | Non-bronchoscopy group (n, details) | Follow-up duration | No. of patients that died | Outcomes reported | Variables matched or adjusted |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Sanchez-Nieto 1998 | Spain | R, OL | Patients with MV and clinically suspected VAP | 51 | 44.2 | 74.5 | 24, PSB and BAL with bronchoscopy to guide the antibiotic regimen | 27, QEA to guide the antibiotic regimen | During hospitalization | 18 | Mortality, MV time, and ICU stay | Age, sex, and APACHE II on admission |
| Fagon 2000 | France | R, OL | Patients with MV and clinically suspected VAP | 413 | 63 | 70 | 204, PSB and BAL with bronchoscopy to guide the antibiotic regimen | 209, NQEA to guide the antibiotic regimen | 28-day | 144 | Mortality, and ICU stay | Age, SAPS II score, and McCabe–Jackson classification, duration of MV before inclusion, ODIN score, and PaO2/FIO2 ratio |
| Ruiz 2000 | Spain | R, OL | Patients with MV and clinically suspected VAP | 76 | 65.9 | 69.7 | 37, PSB and BAL with bronchoscopy to guide the antibiotic regimen | 39, QEA to guide antibiotic the regimen | 30-day | 32 | Mortality, MV time, and ICU stay | Age, sex, causes for ICU admission, and APACHE II on admission |
| Violan 2000 | Spain | R, OL | Patients with MV and clinically suspected VAP | 88 | 52.9 | 72.7 | 45, PSB and BAL with bronchoscopy to guide the antibiotic regimen | 43, NQEA to guide the antibiotic regimen | During hospitalization | 19 | Mortality, MV time, and ICU stay | Age, sex, PaO2/FIO2 ratio, duration of MV before inclusion, and APACHE II on admission |
| CCCTG 2006 | Canada and USA | R, OL | Patients with MV and clinically suspected VAP | 739 | 59 | 69.3 | 365, SB and BAL with bronchoscopy to guide the antibiotic regimen | 374, NQEA to guide the antibiotic regimen | 28-day | 138 | Mortality, MV time, and ICU stay | Age, sex, PaO2/FIO2 ratio, comorbidities, duration of MV before inclusion, and APACHE II on admission |
| Michetti 2012 | USA | PC | Patients with MV and clinically suspected VAP | 137 | 43 | 83.2 | 96, BAL with bronchoscopy to guide the antibiotic regimen | 41, bronchoscopy not used | During hospitalization | 15 | Mortality, MV time, and ICU stay | Age, sex, admission GCS score |
| Guidry 2014 | USA | RC | Patients with culture-confirmed VAP | 493 | 53.7 | 74.6 | 159, diagnostic and/or therapeutic bronchoscopy | 334, bronchoscopy not used | During hospitalization | 89 | Mortality | Age, sex, trauma, transfusion, hospital days before VAP, and APACHE II on admission |
| Wu 2021 | China | R, OL | Patients with culture-confirmed VAP | 100 | 63 | 53 | 50, diagnostic and/or therapeutic bronchoscopy | 50, bronchoscopy not used | During hospitalization | NR | ICU stay | Age and sex |
| Karbasy 2021 | Iran | R, OL | Patients with culture-confirmed VAP | 50 | 46 | 74 | 25, therapeutic bronchoscopy | 25, bronchoscopy not used | During hospitalization | 18 | Mortality | Age, sex, and APACHE II on admission |
| Zhang 2022 | USA | RC | Patients with clinically diagnosed VAP | 1560 | 63.8 | 63.5 | 205, diagnostic and/or therapeutic bronchoscopy | 1355, bronchoscopy not used | During hospitalization | NR | Mortality and MV time | Age, sex, race, BMI, comorbidities, and PaO2/FIO2 ratio |
| Allam 2023 | Egypt | R, OL | Patients with clinically diagnosed VAP | 200 | NR | 77.5 | 100, BAL with bronchoscopy to guide the antibiotic regimen | 100, bronchoscopy not used | During hospitalization | 27 | Mortality | Age, sex, and causes of ICU admission |

R, randomized; OL, open label; PC, prospective cohort; RC, retrospective cohort; MV, mechanical ventilation; VAP, ventilator-associated pneumonia; NR, not reported; PSB, protected specimen brush; BAL, bronchoalveolar lavage; QEA, quantitative endotracheal aspirates; NQEA, non-quantitative endotracheal aspirates; ICU, intensive care unit; APACHE, acute physiology and chronic health evaluation; SAPS II, simplified acute physiology score II; ODIN, organ dysfunction and infection; GCS, Glasgow coma scale; BMI, body mass index.

reasons, as outlined in Fig. 1. Ultimately, 11 studies [21–31] were deemed suitable for inclusion.

### 3.2. Study characteristics and data quality

An overview of the included studies can be found in Table 1. Overall, eight RCTs [21–25,28,29,31] and three cohort studies [26,27,30], comprising 3907 patients with highly suspected or clinically diagnosed VAP, were included in the meta-analysis. These studies were published between 1998 and 2023, and performed in various countries, namely Spain, France, Canada, the United States, China, Iran, and Egypt. The sample sizes of the studies varied from 50 to 1560. The mean ages of the patients were 43–66 years old, and the proportion of men was from 53 % to 83 %. As for the role of bronchoscopy in the intervention groups, bronchoscopy was used only for the purpose of the microbiological diagnosis of VAP to guide the antibiotic regimen in seven studies [21–26,31]; while in the other four studies, bronchoscopy was also used for therapeutic purposes, such as to assist sputum suction [27–30]. The follow-up durations were within the hospitalization duration for eight studies [21,24,26–31], and during 28 or 30 days in the other three studies [22,23,25]. Potential confounding factors, such as age and sex, were matched or adjusted among all the included studies. The details of the study quality evaluation for the RCTs are shown in Table 2. All of the included RCTs were open-label studies. Details of the random-sequence generation were reported in six studies [21–25,31], while details of allocation concealment were reported in five studies [22–25,31]. No other potential risk of bias was observed. Quality evaluation of the included cohort studies is shown in Table 3. The NOS scores were all eight or nine stars, suggesting the studies were of good quality.

### 3.3. Influence of bronchoscopy use on all-cause mortality in patients with VAP

Ten studies reported the outcome of all-cause mortality in patients with VAP [21–28,30,31]. The results of the overall meta-analysis suggested that bronchoscopy use was not associated with a significant influence on all-cause mortality in patients with VAP compared to the controls without the use of bronchoscopy (RR: 0.81, 95 % CI: 0.62 to 1.05, $p = 0.12$; $I^2 = 57$ %; Fig. 2A). Subsequent subgroup analysis according to the study design showed consistent results in the RCTs (RR: 0.88, 95 % CI: 0.70 to 1.10, $p = 0.27$; $I^2 = 24$ %) and cohort studies (RR: 0.65, 95 % CI: 0.32 to 1.33, $p = 0.23$; $I^2 = 77$ %; $p$ for subgroup difference = 0.42; Fig. 2B). Interestingly, subgroup analysis showed that bronchoscopy use for the microbiological diagnosis of VAP was not associated with reduced mortality (RR: 0.92, 95 % CI: 0.75 to 1.13; $p = 0.45$; $I^2 = 22$ %), while therapeutic bronchoscopy use was associated with significantly reduced mortality (RR: 0.53, 95 % CI: 0.35 to 0.81; $p = 0.003$; $I^2 = 22$ %). The effect between subgroups was significant ($p = 0.02$; Fig. 3A). Further subgroup analysis showed consistent results in studies reporting in-hospital mortality, and those reporting 28-day/30-day mortality ($p$ for subgroup difference = 0.98; Fig. 3B).

### 3.4. Influence of bronchoscopy use on MV duration and ICU stay

The pooled results from five studies [21,23–26] did not show any significant difference in MV duration between patients with or without bronchoscopy use (MD: 0.44 days, 95 % CI: −0.33 to 1.21, $p = 0.26$; $I^2 = 16$ %; Fig. 4A). The pooled results from seven studies [21–26,29] showed similar ICU stays between groups (MD: 1.04 days, 95 % CI: −0.09 to 2.18, $p = 0.07$; $I^2 = 50$ %; Fig. 4B).

### 3.5. Publication bias

The funnel plots for the meta-analyses comparing bronchoscopy-assisted treatment versus the controls without the use of bronchoscopy on the mortality, MV duration, and ICU stay are shown in Fig. 5A–**C**. It can be seen that these plots are symmetrical on visual inspection, suggesting a low risk of publication bias in each. Egger's regression tests also suggested a low risk of publication bias ($p = 0.72$) for the outcome of all-cause mortality. Egger's regression tests for the other two outcomes could not be performed because only five and seven studies were included for these outcomes, which were insufficient numbers.

**Table 2**
Study quality evaluation of the included RCTs via the Cochrane Risk of Bias Tool.

| RCTs | Random-sequence generation | Allocation concealment | Blinding of participants | Blinding of the outcome assessment | Incomplete outcome data addressed | Selective reporting | Other sources of bias |
|---|---|---|---|---|---|---|---|
| Sanchez-Nieto 1998 | Low risk | Unclear | High risk | High risk | Low risk | Low risk | Low risk |
| Fagon 2000 | Low risk | Low risk | High risk | High risk | Low risk | Low risk | Low risk |
| Ruiz 2000 | Low risk | Low risk | High risk | High risk | Low risk | Low risk | Low risk |
| Violan 2000 | Low risk | Low risk | High risk | High risk | Low risk | Low risk | Low risk |
| CCCTG 2006 | Low risk | Low risk | High risk | High risk | Low risk | Low risk | Low risk |
| Wu 2021 | Unclear | Unclear | High risk | High risk | Low risk | Low risk | Low risk |
| Karbasy 2021 | Unclear | Unclear | High risk | High risk | Low risk | Low risk | Low risk |
| Allam 2023 | Low risk | Low risk | High risk | High risk | Low risk | Low risk | Low risk |

**Table 3**
Quality evaluation of the included cohort studies via the Newcastle–Ottawa scale.

| Cohorts | Representativeness of the exposed cohort | Selection of the non-exposed cohort | Ascertainment of exposure | Outcome not present at baseline | Control for age and sex | Control for other confounding factors | Assessment of outcome | Sufficiently long follow-up duration | Adequacy of follow-up of the cohorts | Total |
|---|---|---|---|---|---|---|---|---|---|---|
| Michetti 2012 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 9 |
| Guidry 2014 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 8 |
| Zhang 2022 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 8 |

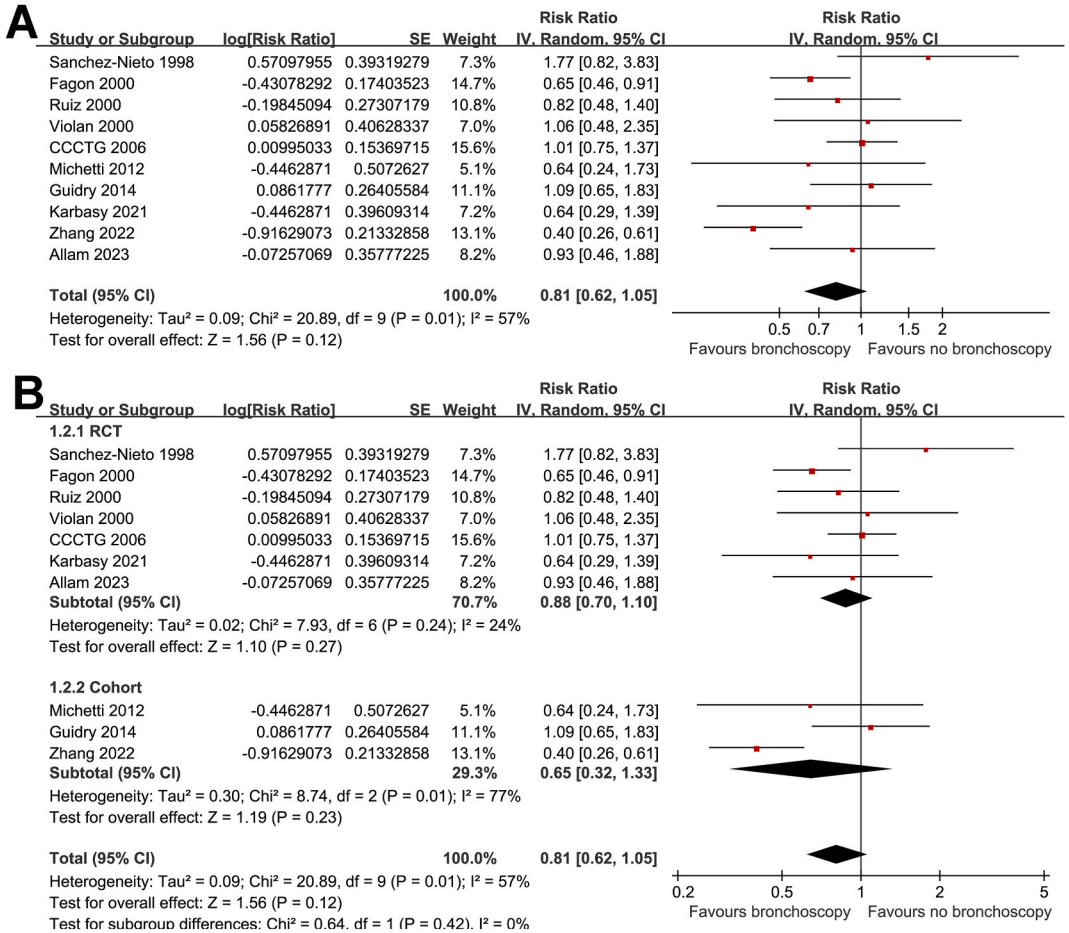


**Fig. 2.** Forest plots for the meta-analysis comparing bronchoscopy-assisted treatment versus controls without the use of bronchoscopy on the risk of all-cause mortality in patients with VAP; A, forest plots for the overall meta-analysis; and B, forest plots for the subgroup analysis according to the study design.

### *3.6. Certainty of evidence assessment using GRADE*

The certainty of evidence about the influence of incorporating bronchoscopy in the management of patients with VAP on all-cause mortality, MV duration, and length of ICU stay was assessed using the GRADE methodology, with the certainty rated as very low for each aspect, primarily because all the included RCTs were open-label studies, which raises concerns about a risk of bias (Table 4).

## 4. Discussion

In this study, we pooled the results of 11 eligible RCTs and cohort studies, and the results showed that overall, compared to a control group without the use of bronchoscopy, incorporating bronchoscopy in the management of patients with VAP was not associated with a reduced risk of all-cause mortality. However, significant heterogeneity was observed, and further subgroup analysis according to the role of bronchoscopy showed that although bronchoscopy use for the diagnosis of the causative pathogens of VAP did not reduce mortality in these patients, bronchoscopy used for therapeutic purposes, such as assisting sputum suction, was associated with a significantly reduced mortality in patients with VAP. Further subgroup analysis according to the study design and follow-up duration showed similar results, and the pooled results showed that the duration of MV or length of ICU stay was not significantly different between groups. Taken together, the results of the meta-analysis suggest that bronchoscopy use for the purpose of the microbiological diagnosis of VAP did not reduce short-term mortality compared to in patients without bronchoscopy use, while therapeutic bronchoscopy use was associated with a reduced mortality in these patients.

To the best of our knowledge, few meta-analyses have comprehensively evaluated the potential role of bronchoscopy use in the management of patients with VAP. An early meta-analysis in 2005 that included four RCTs involving 628 patients showed that, although invasive cultures could be used with bronchoscopy to identify the causative pathogen of VAP, such invasive testing could affect antibiotic use and prescribing in patients with VAP, but the use of bronchoscopy for the microbiological diagnosis of VAP did not

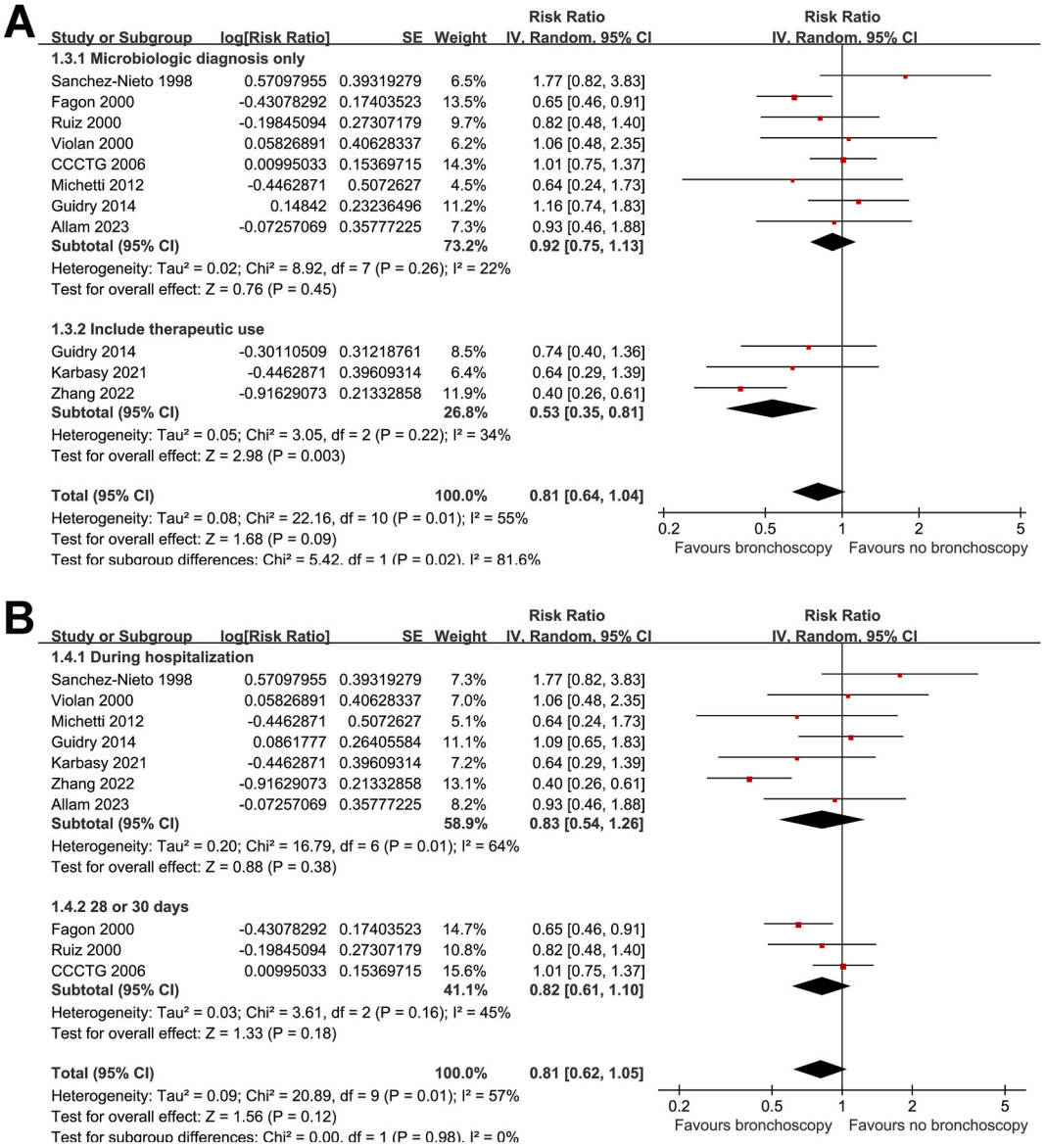


**Fig. 3.** Forest plots for the subgroup analyses comparing bronchoscopy-assisted treatment versus controls without the use of bronchoscopy on the risk of all-cause mortality in patients with VAP; A, forest plots for the subgroup analysis according to the detailed use of bronchoscopy-assisted treatment; and B, forest plots for the subgroup analysis according to the follow-up duration.

significantly alter the mortality of the patients [32]. However, only four studies were available at the time of the meta-analysis, and the authors concluded that few trials had systematically examined the impact of bronchoscopy use on outcomes for patients with suspected or suffering from VAP, and the role of bronchoscopy use in the management of patients with VAP remains not fully determined. Our meta-analysis has several advantages compared to that previous one. First, we performed an updated literature search in three commonly used electronic databases, which enabled us to retrieve 11 up-to-date studies according to the aim of the meta-analysis. Overall, the sample size of the current meta-analysis (3907 patients) was much larger than in the previous one, which enabled us to perform multiple subgroup analyses to determine the sources of heterogeneity. In addition, due to the relatively large number of studies included in our meta-analysis, besides evaluating the influence of bronchoscopy use on all-cause mortality in patients with VAP, we were also able to evaluate changes in other outcomes, such as MV duration, and length of ICU stay. Finally, several subgroup analyses were performed, and we found consistent results with the mortality outcome in RCTs and in cohort studies, and in studies reporting in-hospital and 28-day/30-day mortality outcomes. Interestingly, subgroup analysis showed that the detailed role of bronchoscopy use may affect the results of the meta-analysis. Bronchoscopy use for the purpose of the microbiological diagnosis of VAP only did not reduce short-term mortality, while therapeutic bronchoscopy use was associated with reduced mortality in these patients. Since the heterogeneity of the overall meta-analysis was significant ($I^2 = 57$ %) but became nonsignificant within subgroups ($I^2 = 22$ %

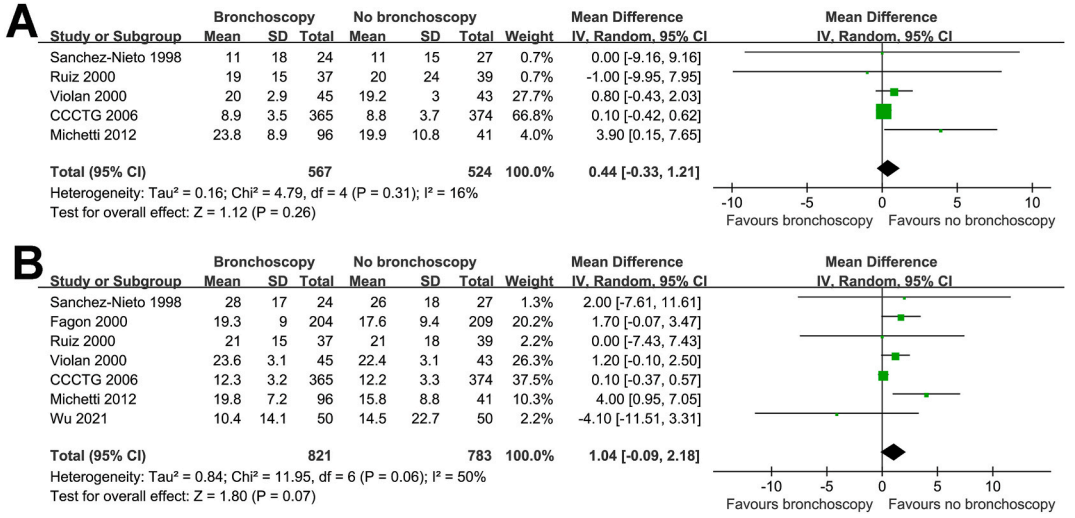


**Fig. 4.** Forest plots for the meta-analyses comparing bronchoscopy-assisted treatment versus controls without the use of bronchoscopy for the MV duration and ICU stay in patients with VAP. A, forest plots for the outcome of the MV duration; and B, forest plots for the outcome of ICU stay.

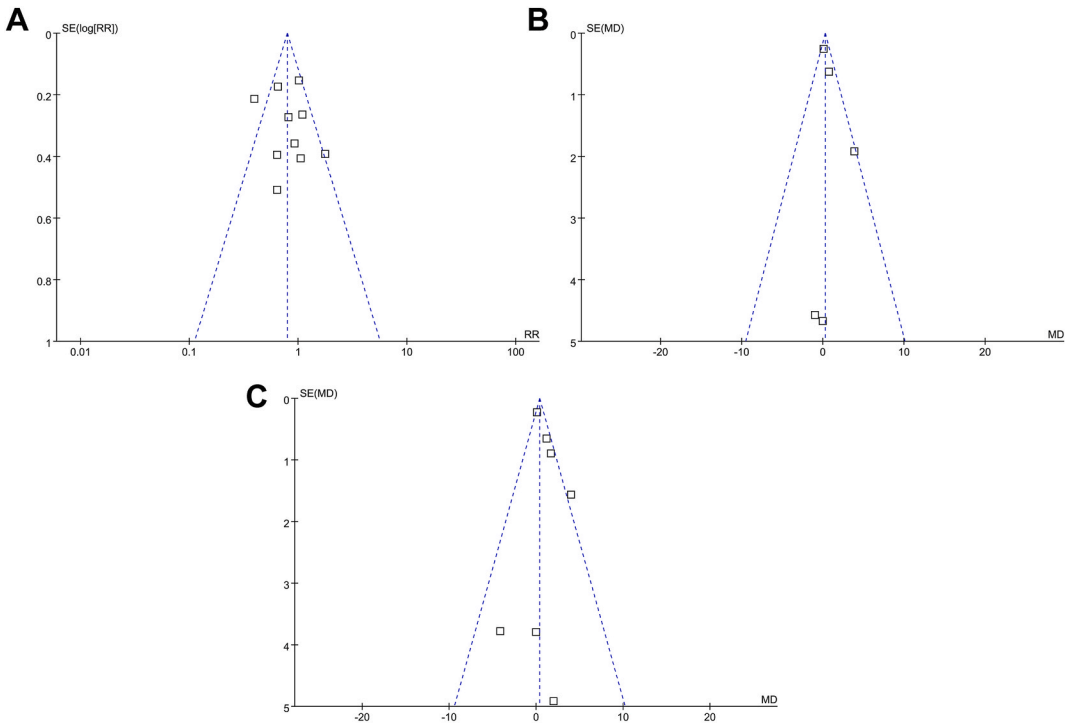


**Fig. 5.** Funnel plots for the meta-analysis evaluating the publication biases of the meta-analyses. A, funnel plots for the outcome of all-cause mortality; B, funnel plots for the outcome of MV duration; and C, forest plots for the outcome of ICU stay.

and 34 %), respectively, this indicates that the different role of bronchoscopy use for the management of VAP may explain the source of the heterogeneity.

The results of the current meta-analysis regarding the mortality outcome in patients with VAP are consistent with the previous meta-analysis, which showed that the use of bronchoscopy for the microbiological diagnosis of VAP did not significantly alter the mortality of the patients [32]. These findings could also be elucidated by the utilization of initial antimicrobial therapy, which is usually guided by local patterns of microorganism prevalence and antibiotic susceptibility, which can aid in the development of empirical strategies with a higher rate of appropriateness for the treatment of patients with VAP [33]. In the case of patients with VAP, knowledge regarding the microorganisms involved and their sensitivities to antibiotics indicates that empirical antibiotic therapy

**Table 4**
Summarized certainty of evidence using the GRADE system.

| Outcome | Quality assessment | | | | | | | Absolute effect | Certainty |
|---|---|---|---|---|---|---|---|---|---|
| | No. of studies | Design | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | | |
| All-cause mortality | 10 | RCTs and cohort studies | Serious[a] | Serious[b] | Not serious | Not serious | None | RR (95 % CI): 0.81 (0.62–1.05) | ⊕OOO Very low |
| Duration of MV | 5 | RCTs and cohort studies | Serious[a] | Not serious | Not serious | Not serious | None | MD (95 % CI): | ⊕OOO Very low |
| Length of ICU stay | 7 | RCTs and cohort studies | Serious[a] | Serious[c] | Not serious | Not serious | None | MD (95 % CI): | ⊕OOO Very low |

Explanations.
GRADE, Grading of Recommendations, Assessment, Development, and Evaluation; MV, mechanical ventilation; ICU, intensive care unit; RCTs, randomized controlled trials; RR, risk ratio; MD, mean difference; CI, confidence interval.
[a] all of the included RCTs were open-label studies.
[b] $I^2 = 57$ %, indicating moderate heterogeneity.
[c] $I^2 = 50$ %, indicating moderate heterogeneity.

would be suitable [33]. Consequently, it is logical to infer that understanding the local patterns of microorganisms holds greater significance than the techniques employed for the collection and cultivation of respiratory samples. On the other hand, the results of the subgroup analysis suggested that therapeutic bronchoscopy use, such as assisting sputum suction, was associated with significantly reduced mortality in patients with VAP. These results were consistent with the previously observed benefits of therapeutic bronchoscopy in patients with aspiration pneumonia [9] and refractory pneumonia [34], and highlight the potential importance of optimized airway management in patients with VAP. However, the results should be interpreted with some caution because only three studies were available for inclusion in the therapeutic bronchoscopy use subgroup, and only one of them was an RCT [28]. More large-scale RCTs are thus needed to validate this finding.

### *4.1. Limitations*

Our study also possesses certain limitations that should be noted. First, the meta-analysis relied on non-blinded RCTs and cohort studies, and accordingly, the certainty of evidence was rated as very low in accordance with the GRADE methodology, necessitating the inclusion of high-quality double-blinded RCTs to authenticate the findings. Nevertheless, conducting blinded studies in this particular clinical scenario using bronchoscopy is challenging. Additionally, the proficiency of the physicians performing the bronchoscopy and BAL might impact the outcomes of the meta-analysis, and thus warrants evaluation in future investigations. Moreover, determination of the optimal protocol and frequency of therapeutic bronchoscopy in patients with VAP remains unresolved. Additionally, it is worth noting that the limited number of studies encompassing the use of therapeutic bronchoscopy, particularly in assisting sputum suction, necessitates large-scale clinical trials to validate the conclusion that such interventions are significantly associated with reduced mortality in patients with VAP.

## 5. Conclusions

In conclusion, the results of the present meta-analysis indicate that although bronchoscopy use for the purpose of the microbiological diagnosis of VAP did not reduce short-term mortality in patients compared to in those without bronchoscopy use, therapeutic bronchoscopy use, such as for assisting sputum suction, may reduce short-term mortality in patients with suspected or suffering from VAP. Large-scale high-quality RCTs are needed to validate the findings of this meta-analysis and to determine the optimal protocol and frequency of therapeutic bronchoscopy in patients with VAP.

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## Data availability statement

All data generated or analyzed during this study are included in the article; further inquiries can be directed to the corresponding author.

## CRediT authorship contribution statement

**Fei Tang:** Writing – original draft, Software, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Feng Zhu:** Writing – original draft, Data curation. **Yueming Wang:** Software, Methodology, Formal analysis. **Xiankui Zha:** Software, Methodology, Formal analysis, Conceptualization. **Liping Lyu:** Software, Methodology, Funding acquisition, Formal analysis. **Dongchun Ma:** Writing – review & editing, Supervision, Project administration, Conceptualization.

## Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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None.

## Abbreviations

| | |
|---|---|
| VAP | Ventilator-associated pneumonia. |
| MV | mechanical ventilation. |
| ICU | intensive care unit. |
| BAL | bronchoalveolar lavage. |
| RCTs | randomized controlled trials. |

NOS Newcastle–Ottawa scale.

## Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2024.e32751.

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