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Review Article

Risk Factors for Ventilator-Associated Pneumonia in Elderly ICU Patients: A Meta-Analysis

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Abstract

Background: To systematically evaluate the risk factors of ventilator-associated pneumonia (VAP) in critically ill elderly patients in intensive care unit (ICU).

Methods: The China National Knowledge Infrastructure (CNKI), Wanfang Database, PubMed and Web of science databases were searched to collect the literature published at home and abroad on the risk factors of ventilator-associated pneumonia in critically ill elderly patients in ICU. The publication date of the literature was up to Oct 24, 2024. Meta-analysis was performed using Stata SE14.0 software to calculate the Odds ratio (OR) and 95% Confidence intervals (CIs) of each risk factor.

Results: Thirteen articles were included, all of which were case-control studies. Age, glucocorticoids, mechanical ventilation ≥7 d, tracheotomy, gastrointestinal feeding nutrition, and acute physiological and acute physiology and chronic health evaluation ii(APACHEII) score ≥15 were the risk factor for VAP in ICU patients (OR (95%CI) were 1.044 (1.004, 1.086), 4.663 (2.098, 10.363), 2.749 (1.912, 3.952), 7.405 (2.040, 26.884), 2.676 (1.888, 3.794), 1.822 (1.198, 2.771).

Conclusion: Clinical interventions targeting age, glucocorticoid use, mechanical ventilation ≥7 days, tracheotomy, gastrointestinal feeding nutrition, and APACHEII ≥15 should be prioritized to reduce VAP incidence in critically ill elderly ICU patients.

Keywords: Elderly; Ventilator-associated pneumonia; Risk factors; Meta-analysis

Introduction

Most of the elderly patients in intensive care unit (ICU) are in critical condition, and endotracheal intubation and mechanical ventilation are needed to maintain airway patency and prevent inhalation, thus improving the oxygenation state of the body (1). Such supportive interventions are an important part of the clinical treatment of elderly ICU patients. However, tracheal intubation may cause many complications, which may pose a significant risk to elderly ICU patients (2). Tracheal intubation and mechanical ventilation may cause airway mucosal injury, venous thromboembolism, lung injury or atelectasis, elevated intracranial tension, cardiovascular disease and nosocomial pneumonia in elderly ICU patients (2, 3). Ventilator-associated pneumonia (VAP), which is a

common infectious disease in elderly ICU patients with severe disease, is caused by mechanical ventilation of ventilator (4). About 14%-27% of ICU patients will suffer from VAP, which poses a fatal threat to the life and health of patients. Studies have shown that the mortality rate of ICU patients with VAP is doubled compared with that of ICU patients without VAP (5). Since there is still a lack of effective treatment for VAP, it is of great clinical value to take intervention measures to prevent the occurrence of VAP in the early stage.

Previous studies have discussed the risk factors of VAP, and found that VAP is the result of the combined action of multiple risk factors, and the patient's age, underlying diseases and non-standard use of antibiotics can all lead to the occurrence of VAP (6). However, these studies are often limited by sample size, resulting in low research efficiency. Therefore, this study intends to collect and evaluate relevant literature, and use meta-analysis system to explore the risk factors of VAP, so as to provide evidence for early clinical intervention measures.

Materials and Methods

Literature search

We systematically searched PubMed database, Web of Science database, China National Knowledge Infrastructure (CNKI) database and Wanfang Data platform. The search term is a combination of subject word and free word. The English search words included "ICU", "intensive care", "intensive care unit", "risk factor", "risk factor hazards", "VAP", "ventilator associated" pneumonia ", "severe" and "critical". The Chinese search terms included "ICU", "intensive care unit", "intensive care unit", "risk factors", "influencing factors", "related factors", "VAP", "ventilator pneumonia", "ventilator associated pneumonia", "severe patients" and "critically ill patients", etc. As of October 24, 2024, the language is limited to Chinese and English.

From Chinese and English databases, 2370 literatures were retrieved. After eliminating 247 duplicates, 65 meta - analyses/reviews, 1262 unrelated papers, 596 on mild/early - stage patients, and 187 with unavailable data, 13 references were included in the meta - analysis (7-19). All were case - control studies with NOS scores ≥7. (Table 1, Fig. 1)

Table 1: Basic characteristics and quality evaluation of the included literatures

No	First author	Year	Sample size (cases)		Research factor	NOS score
			Case group	Control group		
1	Shi (7)	2020	41	94	⑤⑨	7
2	Wang (8)	2022	48	166	①④⑤⑦⑧⑨	7
3	Wu (9)	2022	23	63	①④⑤⑥	7
4	Zhong (10)	2022	43	61	③	8
5	Zhang (11)	2021	56	122	①⑤⑧	7
6	Wang (12)	2017	36	44	③⑤	8
7	Ma (13)	2024	45	45	⑤⑨	7
8	Kong (14)	2021	63	50	①②	7
9	Zhao (15)	2017	72	90	⑨	8
10	Liu (16)	2022	58	55	①⑥	8
11	Karatas (17)	2016	178	974	②③⑦⑧	8
12	Reyes LF (18)	2023	610	2677	①	7
13	Deye N (19)	2024	33	128	①②⑨	7

Note: ① Age; ② Gender; ③ The use of antibiotics; ④ Use glucocorticoid; ⑤Mechanical ventilation time ≥7 d; ⑥Tracheotomy; ⑦Gastrointestinal feeding nutrition; ⑧Pre-existing COPD; ⑨APACHEII scores ≥15.

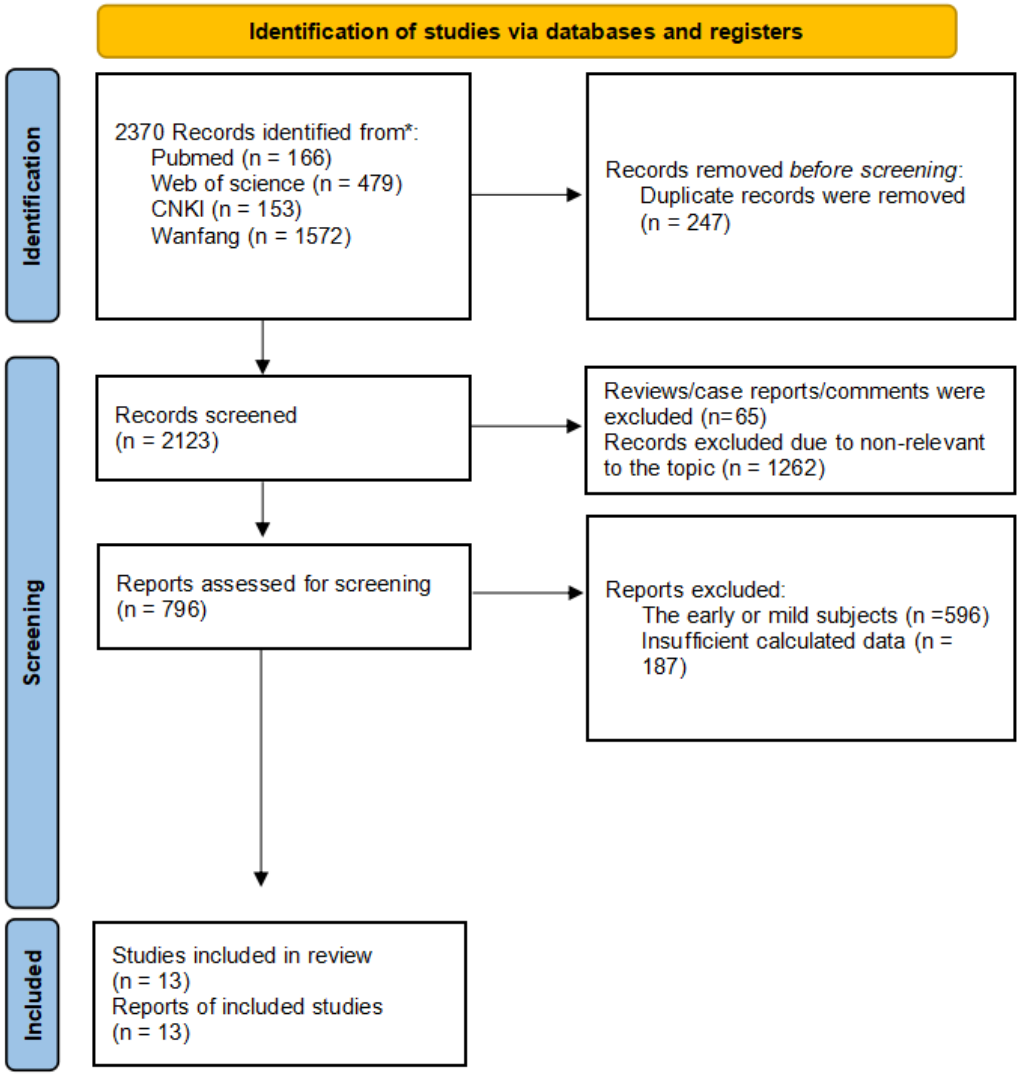

Fig. 1: Flow chart of literature screening

Inclusion and exclusion criteria

All included literatures were required to meet the following criteria:

1) Study subjects were critically ill elderly patients in ICU, ≥65 years of age, without ethnic restriction;
2) Case-control or cohort studies including VAP group and non-VAP group. The diagnostic criteria for VAP were based on the Guidelines for Diagnosis, Prevention and Treatment of Ventilators Associated Pneumonia (20);
3) Outcome indexes were VAP risk factors;
4) The Odds ratio (OR) and 95% Confidence intervals (CIs) are provided in the original literature.
5) RCT studies.

If the literature contained one of the following criteria, it was excluded:

1) meta-analysis, review, case analysis, review;
2) Animal and cell research;
3) No OR value and 95%CIs are provided;
4) repeated publication of papers;
5) small sample size.

Literature data extraction and quality evaluation

The literatures were screened strictly according to the inclusion and exclusion criteria, and the relevant data were extracted. Data extraction included the name of the first author, year of publication, country of study, type of study design, sample size, and risk factors associated with the study. Meanwhile, Newcastle-Ottawa Scale (NOS) was used to evaluate the quality of the included literature (21). The full score of the scale is 9 points, and the scores of 1-3, 4-9 and 7-9 are high risk, medium risk and low risk studies respectively. The above process is completed independently by two researchers. In case of any discrepancy, both parties shall discuss it or consult a third-party expert for advice.

Statistical Analysis

Meta-analysis was performed using STATA14.0 statistical software (StataCorp, College Station, TX). The data were tested for heterogeneity. Heterogeneity test was evaluated using I2 (the proportion of variation in heterogeneity to total variation). The random effects model was used for meta-analysis. The combined effect size of each study was expressed by the OR value and 95%CIs, with the test level α=0.05. Begg's rank correlation method was used to test publication bias. The sensitivity analysis was conducted by one-by-one elimination method, and the results of meta-analysis before and after elimination were compared. If the effect size changes greatly after a study is excluded, it suggests that the excluded study may be the main source of heterogeneity.

Ethics approval and consent to participate

The authors are 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. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). As this study involves the summary and analysis of other studies, it does not involve medical ethics approval or patient-informed consent.

Results

Analysis of risk factors for VAP in ICU patients

Age

Age as a risk factor for VAP in ICU patients was included in 7 studies (8,9,11,14,16,18,19). This meta-analysis had significant heterogeneity (I^2=81.6%), and the risk of VAP development was significantly higher when combined using a random-effects model (OR (95% CI) =1.044(1.004, 1.086), *P*=0.03, Fig. 2).

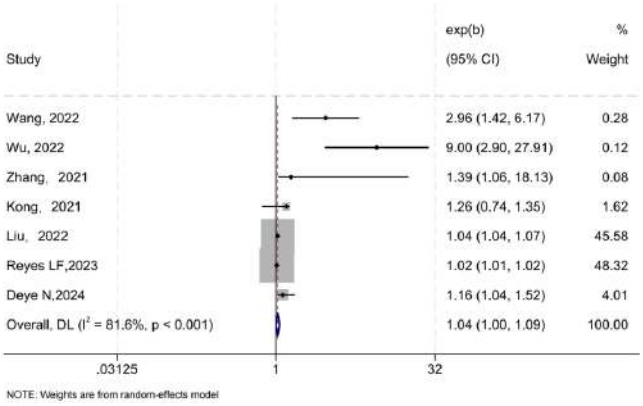

Fig. 2: Meta-analysis forest map of age and risk of VAP in ICU patients

Gender

Three studies (14,17,19) examined the effect of gender on VAP in ICU patients with severe illness. Gender was not significantly associated with the risk of VAP (OR (95%CI)= 1.135 (0.924,1.394), P=0.227, Fig. 3).

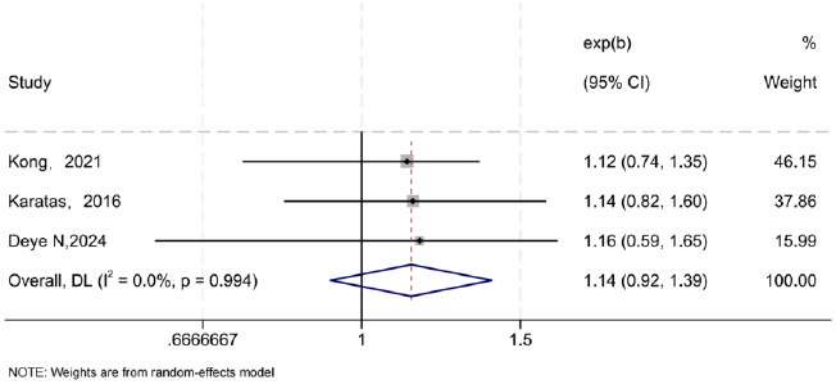

Fig. 3: Meta-analysis forest map of gender and risk of VAP in ICU patients

Use of antibiotics

Three studies (10,12,17) reported the effect of antibiotic use on VAP in ICU patients with severe illness. The risk of VAP was not significantly associated with antibiotic use (OR (95%CI)= 1.135 (0.924，1.394), *P*=0.227, Fig. 4).

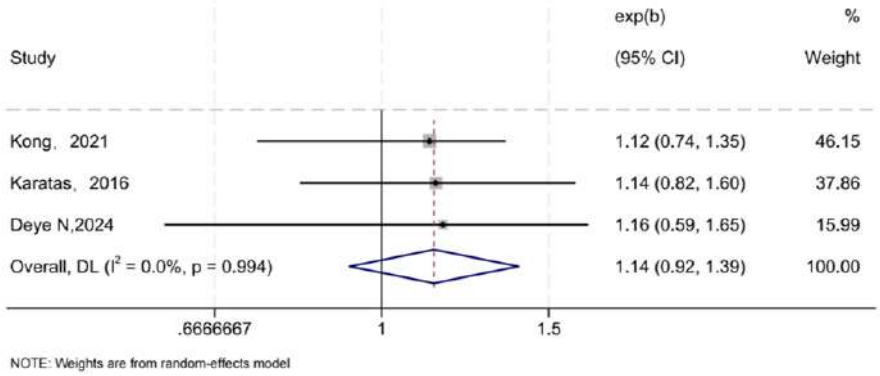

Fig. 4: Meta-analysis forest map of antibiotic use and risk of VAP in ICU patients

Use of glucocorticoids

Two studies (8-9) reported the effect of antibiotic use on VAP in ICU patients with severe illness. The risk of VAP was significantly higher in subjects who used glucocorticoids compared with those who did not (OR (95%CI)= 4.663 (2.098，10.363), *P*<0.001, Fig. 5).

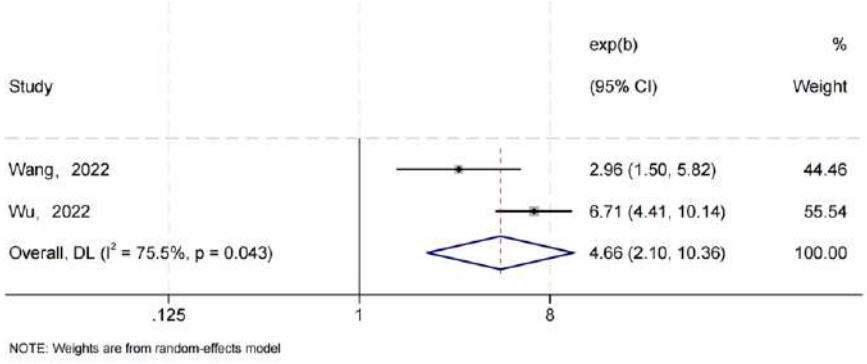

Fig. 5: Meta-analysis forest map of glucocorticoid use and risk of VAP in ICU patients

Mechanical ventilation time ≥7 days

Six studies (7-9,11-13) examined the effect of mechanical ventilation duration ≥7 d on VAP in ICU patients with severe illness. The results of the studies found no significant association with the risk of developing VAP in the study subjects with tracheotomy (OR (95% CI) = 2.749 (1.912, 3.952), *P*<0.001, Fig. 6).

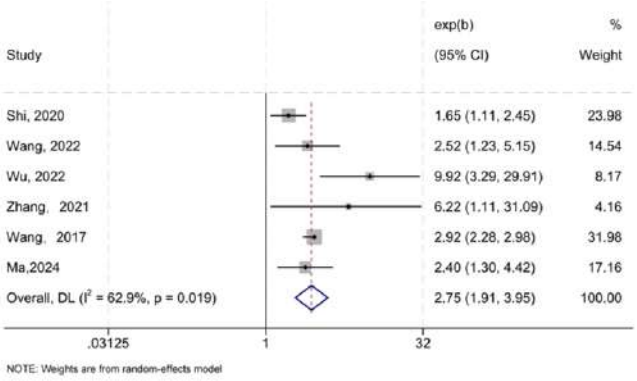

Fig. 6: Meta-analysis forest map of mechanical ventilation duration ≥7 d and risk of VAP in ICU patients

Tracheotomy

Two studies (9,16) reported the effect of tracheotomy on VAP in ICU patients with severe illness. The results of the study found that subjects undergoing tracheotomy had a significantly increased risk of VAP (OR (95% CI)= 7.405 (2.040, 26.884), *P*=0.02, Fig. 7).

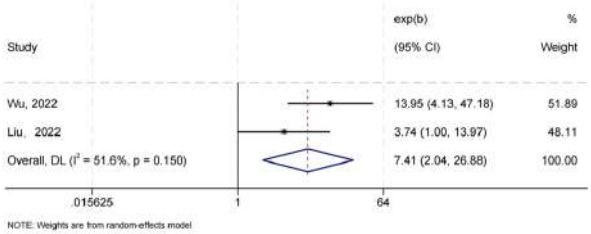

Fig. 7: Meta-analysis forest map of tracheotomy and risk of VAP in ICU patients

Gastrointestinal feeding nutrition

Two studies (8,17) reported the effect of gastrointestinal feeding nutrition on VAP in ICU patients with severe illness. The results of the study found that receiving gastrointestinal feeding nutrition significantly increased VAP risk (OR (95% CI) = 2.676 (1.888, 3.794), *P*<0.001, Fig. 8)

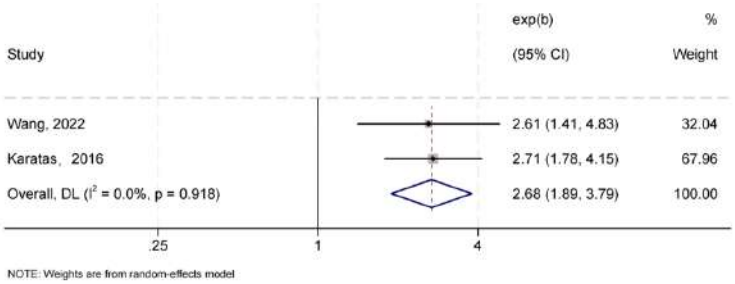

Fig. 8: Forest map of meta-analysis of gastrointestinal feeding nutrition and risk of VAP in ICU patients

Pre-existing chronic obstructive pulmonary disease (COPD)

Three studies (8,11,17) reported the effect of pre-existing COPD on VAP in ICU patients with severe disease. No significant association was found between pre-existing COPD and VAP risk (OR (95%CI)= 2.358 (0.956, 5.817), *P*=0.063, Fig. 9).

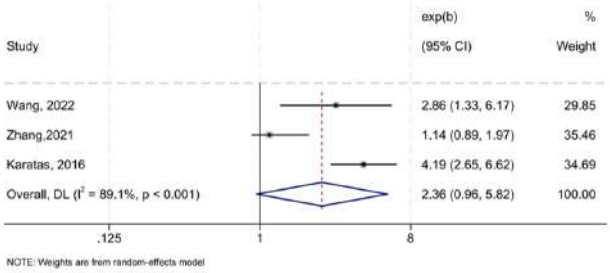

Fig. 9: Meta-analysis forest map of VAP risk in patients with pre-existing COPD and ICU

Acute physiological and acute physiology and chronic health evaluation II (APACHEII) ≥15 points

Five studies (7-8,13,15,19) reported the effect of APACHEII score ≥15 on VAP in ICU patients with severe illness. Subjects with APACHEII score ≥15 had a significantly higher risk of VAP (OR (95%CI) = 1.822 (1.198, 2.771), *P*=0.005, Fig. 10).

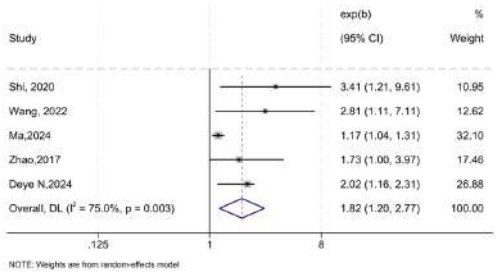

Fig. 10: Meta-analysis forest map of APACHEII score ≥15 and risk of VAP in ICU patients

Analysis of publication bias and sensitivity

Taking mechanical ventilation time as an example, publication bias detection and sensitivity analysis were conducted. The results are shown in Fig. 11, with no significant deviations in the effect intervals, suggesting that the results of the meta-analysis are robust and reliable.

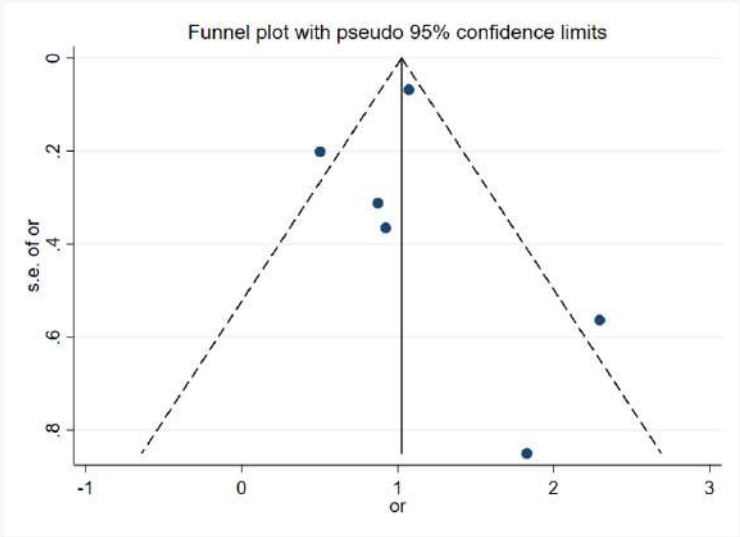

Fig. 11: Sensitivity analysis

Discussion

VAP is a common and serious complication in ICU patients with complex and diverse pathogenesis. VAP usually refers to the substantial lung inflammation caused by mechanical ventilation for 48 h, which has a high fatality rate and seriously affects the prognosis of patients (22). In this study, we conducted a meta-analysis of related studies on VAP risk factors in ICU patients with severe illness. The meta-analysis included 13 case-control studies with 1306 cases and 4569 controls. The results showed that age, glucocorticoids, mechanical ventilation duration ≥7 d, tracheotomy, gastrointestinal feeding nutrition, APACHEII score ≥15 points were risk factors for ICU patients with VAP, and scientific intervention measures could be carried out for related risk factors. To reduce the incidence of VAP in ICU patients, healthcare providers need to be more vigilant in recognizing these risk factors during patient care. Early identification and appropriate intervention can potentially mitigate the impact of these risk factors and thus decrease the likelihood of VAP development.

Elderly patients suffer from many basic diseases, relatively low body resistance, functional decline of various organs, and weakened ciliary movement and clearance function of respiratory tract, and are prone to VAP (23). As we age, the function of the respiratory mucosal barrier weakens and protective mechanisms such as the cough reflex may decline, making it easier for pathogens to invade the respiratory tract and cause infection. Therefore, the monitoring of vital signs of elderly patients in ICU should be increased, which is conducive to reducing the occurrence of VAP. Studies have shown that VAP is often caused by multidrug-resistant pathogens, including *Acinetobacter* spp., *P. aeruginosa, S. aureus*, and *K. pneumoniae*, which are commonly isolated from patients with HAP or VAP in Asian countries (24-25). The use of glucocorticoids can have adverse effects on the body's defense system, promote the imbalance of bacterial flora, cause fungal infection, and increase the risk of VAP.

Therefore, it is necessary to pay attention to aseptic operation in clinic, and standardize the use of glucocorticoids. Prolonged mechanical ventilation and tracheotomy disrupt the patient's respiratory defense system, making it easier for bacteria to enter the lower respiratory tract. Comatose patients have low body resistance and are unable to clear sputum voluntarily, increasing the risk of infection. Gastrointestinal feeding can improve the retention of gastric contents and promote the absorption of nutrients. But it also increases the possibility of reflux and aspiration. The higher the APACHEII score, the worse the autoimmune ability and the higher the risk of VAP. One study retrospectively analyzed data from 121 patients injured by mechanical ventilation-associated pneumonia in the intensive care unit and found that VAP was more likely to occur in specific populations, with a risk of malnutrition. Leukocyte levels and epidemiologic factors were associated with the time of VAP onset, and different pathogenic infections and APACHE II scores affected the chance of late VAP, suggesting that the development of VAP is influenced by multiple factors, and that monitoring these factors is critical for prevention and treatment (26). Additionally, a study has also indicated that improper use of large volumes or multiple broad-spectrum antibiotics may cause microbial dysbiosis, thereby inducing VAP [27], although antibiotic use was not identified as a significant risk factor in the present meta-analysis.

In this meta-analysis, the relationship between different risk factors and VAP was fully considered, and sensitivity analysis was used to exclude one by one, making the results more comprehensive and reliable. However, there are still the following disadvantages. First, the number of included articles for some factors is limited, and their statistical efficacy may be low. Second, significant heterogeneity can be observed during meta-analysis, which may reduce the reliability of the results.

This meta-analysis of 13 case-control studies confirmed multiple significant risk factors for ventilator-associated pneumonia (VAP) in critically ill ICU patients, including age, glucocorticoids, mechanical ventilation duration ≥7 days, tracheotomy, gastrointestinal feeding nutrition, and APACHE II score ≥15. Scientific interventions targeting these specific risk factors effectively reduce VAP incidence. Particular vigilance should be directed toward elderly patients, those receiving glucocorticoids, patients undergoing tracheotomy or enteral feeding, and those requiring prolonged mechanical ventilation. Implementation of standardized ventilator management protocols, optimization of enteral feeding practices, and timely identification of high-risk patients remain crucial for VAP prevention.

Journalism Ethics considerations

Ethical issues (Including plagiarism, informed consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc.) have been completely observed by the authors.

Acknowledgements

Not applicable.

Data availability statement

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Conflicts of Interest

The authors have no conflicts of interest to declare.

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