Original Article

Prevalence and risk factors for ventilator-associated pneumonia after cardiac surgery: a systematic review and meta-analysis

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Background: There is currently significant variation in the reported incidence of ventilator-associated pneumonia (VAP) among postoperative cardiac patients. Moreover, the risk factors for VAP in postoperative cardiac patients remain controversial. This study aims to assess the incidence and risk factors of VAP in postoperative cardiac patients to provide a basis for further prevention and treatment of VAP.

Methods: We systematically reviewed PubMed, EMBASE, and Cochrane Library databases to select studies that met the inclusion criteria until November 2023.

Results: Fifteen studies involving 10,478 patients who underwent cardiac surgery were selected for meta-analysis. The incidence of VAP in postoperative cardiac patients was 10%. The preoperative risk factors for VAP after cardiac surgery included age >70 years, chronic obstructive pulmonary disease (COPD), peripheral vascular disease, renal disease, and severe pulmonary hypertension. Furthermore, the perioperative risk factors for VAP after cardiac surgery included emergency surgery, redo surgery, airway instrumentation, gastric aspiration, reintubation, mechanical ventilation duration >3 days, intra-aortic balloon, New York Heart Association >3, American Society of Anesthesiologists >3, need for transfusion during surgery, and ascending aortic surgery.

Conclusions: The incidence of VAP after cardiac surgery was found to be 10%, and the comprehensive risk factors for VAP were identified, emphasizing the critical need for targeted interventions, including optimization of preoperative health and refined surgical protocols, to effectively reduce the occurrence of VAP in postoperative cardiac patients.

Keywords: Ventilator-associated pneumonia (VAP); cardiac surgery; prevalence; risk factor; meta-analysis

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Introduction

Ventilator-associated pneumonia (VAP) is one of the most common infections in the intensive care unit (ICU). It is also one of the most common types of hospital-acquired infections in postcardiac surgery patients (1,2). Studies have indicated that the reported incidence of VAP after cardiac surgery ranges from 2.1% to 13%, with an occurrence rate of 17.1 to 34.5 cases per 1,000 ventilator days (3). VAP can lead to various adverse events, including aspiration, atelectasis, and pulmonary edema, which can increase morbidity, length of hospital stay, and medical costs in mechanically ventilated patients (4). Moreover, cardiac surgery involves hypothermic anesthesia and cardiopulmonary bypass, which can cause significant surgical trauma. Once VAP occurs postoperatively, the mortality rate significantly increases.

The prevalence of VAP after cardiac surgery varies across studies, with an incidence as high as 24.2% (5). Moreover, exploring the risk factors for postoperative VAP in patients undergoing cardiac surgery will help in implementing early preventive measures. Interventions targeting the modifiable risk factors can reduce the incidence of VAP. Meanwhile, identifying high-risk patients based on non-modifiable risk factors can assist in strengthening preventive strategies. A previous meta-analysis identified the risk factors for VAP after cardiac surgery and found that the risk of VAP could be affected by pulmonary hypertension, chronic obstructive pulmonary disease (COPD), peripheral vascular disease, renal disease, New York Heart Association cardiac function class IV, emergency surgery, intra-aortic balloon counterpulsation, cardiopulmonary bypass time, aortic cross-clamp time, mechanical ventilation time, reintervention, and reintubation (6). However, most results were primarily based on three to four included studies, and the conclusions drawn were not stable. Considering the large number of relevant studies published in recent years, we performed a systematic review and meta-analysis to assess the incidence rate and risk factors of VAP after cardiac surgery. We present this article in accordance with the PRISMA reporting checklist (available at https://jtd.amegroups.com/article/view/10.21037/jtd-24-324/rc) (7).

Highlight box

Key findings

- The incidence of ventilator-associated pneumonia (VAP) after cardiac surgery was found to be 10%, and the risk factors for VAP included age >70 years, chronic obstructive pulmonary disease, peripheral vascular disease, renal disease, severe pulmonary hypertension, emergency surgery, redo surgery, airway instrumentation, gastric aspiration, reintubation, mechanical ventilation duration >3 days, intra-aortic balloon, New York Heart Association >3, American Society of Anesthesiologists >3, need for transfusion during surgery, and ascending aortic surgery.

What is known and what is new?

- The prevalence of VAP after cardiac surgery varies across studies, with an incidence as high as 24.2%.
- The risk factors identified in this study included preoperative and perioperative risk factors.

What is the implication, and what should change now?

- This study reported that the incidence of VAP after cardiac surgery was found to be 10%, and preoperative and perioperative risk factors were identified.
- The modifiable risk factors should be intervened to reduce the occurrence of VAP in postoperative cardiac patients.

Methods

Literature search and selection criteria

Studies reporting the incidence of VAP or risk factors for VAP after cardiac surgery were eligible for inclusion in this study, and the publication language was restricted to English and Chinese. To retrieve literature from PubMed, EMBASE, and Cochrane Library databases up to November 2023, we used the following medical subject headings (MeSH terms) and keywords: ("Ventilator-associated pneumonia" OR VAP OR "Pneumonia, Ventilator-Associated" [MeSH] OR "Pneumonia, Ventilator-Associated/epidemiology" [MeSH]) AND ("Cardiac surgery" OR "Cardiac surgical patient" OR "Cardiac surgical patients" OR "heart surgery" OR "cardiovascular surgery" OR CCU OR CICU OR "cardiac intensive care unit" OR "Thoracic Surgery" [MeSH] OR "Cardiac Surgical Procedures" [MeSH] OR "myocardial revascularization" [MeSH] OR "Coronary Care Units" [MeSH]). Additionally, we manually searched the reference lists of potentially relevant studies to identify new studies that met the inclusion criteria.

Two authors independently conducted the literature search and selection. When there were discrepancies in the results, the corresponding author decided whether to include the study by consulting the relevant references. The specific inclusion criteria were as follows: (I) patients: adult patients undergoing cardiac surgery; (II) exposure: risk factors should be reported ≥ two studies; (III) outcomes: the incidence of VAP or effect estimate for the risk of VAP; and (IV) study design: retrospective case-control and prospective studies.

Data extraction and quality assessment

Data extraction from the included studies was independently conducted by two authors. When discrepancies were observed in the extracted results, the corresponding author consulted the relevant literature to determine the final content. The primary information extracted included the first author's name, publication year, region, study design, sample size, age, male proportion, duration of mechanical ventilation, type of cardiac surgery, definition of VAP, adjusted levels, and reported effect estimates. The Newcastle-Ottawa Scale (NOS), which has been partially

validated for assessing the quality of observational studies in meta-analyses, was used to assess the methodological quality of the included studies (8). The NOS comprises three domains, as follows: selection, comparability, and outcome. A set of eight items with a maximum rating of nine stars was devised to evaluate quality. Quality assessment of the individual studies was conducted by two independent authors, and any disagreements between them were resolved by a third author, who thoroughly examined the full text of the article.

Statistical analysis

The random-effects models with a logit transformation were utilized to aggregate the overall incidences of VAP, and the restricted maximum likelihood estimation was employed to fit all models by applying a classic continuity correction of 0.5 for zero cells and sample sizes (9). Odds ratios (ORs) with 95% confidence intervals (CIs) were used to explore potential risk factors for VAP after cardiac surgery, and pooled analyses were performed using random effects models (9,10). The continuous variables between VAP and non-VAP were assigned as weighted mean difference (WMD), and pooled effect estimate with 95% CI were calculated by using the random-effects model (9,10). Heterogeneity among the included studies was assessed using I^2 and Q statistics, and significant heterogeneity was defined as I^2>50.0% or P<0.10 (11,12). Sensitivity analyses were performed to assess the stability of the pooled conclusions by sequentially removing a single study (13). Subgroup analyses for the VAP rate were also performed according to region, and the differences between subgroups were compared using the interaction *t*-test, which assumes that the data were normally distributed (14). Publication bias was assessed using both qualitative and quantitative methods, including funnel plots, Egger's test, and Begg's test (15,16). The significance level for pooled outcomes was set at 0.05, and all P values were calculated using a two-sided test. Statistical analyses were performed using the STATA software (version 12.0; Stata Corporation, College Station, TX, USA).

Results

Search of the literature

The database search yielded 1,146 articles, of which 593 duplicate studies were excluded. Of the remaining 553 studies, 455 were deemed irrelevant. We conducted a full-text review of the remaining 98 articles and excluded 83 studies, primarily for the following reasons: non-cardiac surgical patients (n=28), pediatric patients (n=36), and no relevant results (n=19). Finally, the remaining 15 studies were selected for final meta-analysis; the details of literature search and study selection are shown in *Figure 1* (17-31).

Characteristics of the included studies

Characteristics of the included studies and patients are shown in *Table 1*. Of the 15 included studies, 10 were prospective cohort studies, 2 were retrospective cohort studies, 2 were case-control studies, and the remaining 1 was a cross-sectional study. These studies included 10,478 patients who underwent cardiac surgery and 786 patients with VAP. Ten studies were conducted in Europe or America, and the remaining five were conducted in Asia. Study quality was assessed using the NOS as follows: four studies with eight stars, five studies with seven stars, and six studies with six stars.

Incidence of VAP

Fourteen studies reported the incidence of VAP after cardiac surgery, and the pooled incidence of VAP was 10% (95% CI: 4–12%; P<0.001; *Figure 2*). Moreover, significant heterogeneity was observed across the included studies (I^2=95.5%, P<0.001). Sensitivity analysis revealed that the pooled incidence of VAP ranged from 8% to 10% after sequential removal of a single study (data not shown). Subgroup analyses revealed that the incidence of VAP in Europe, America, and Asia was 10% (95% CI: 6–13%; P<0.001), 13% (95% CI: 6–21%; P=0.001), and 8% (95% CI: 4–12%; P<0.001), respectively.

Preoperative risk factors for VAP

A summary of the preoperative risk factors for VAP after cardiac surgery is shown in *Figure 3*. We noted age >70 years (OR =4.09; 95% CI: 2.55–6.54; P<0.001), COPD (OR =1.66; 95% CI: 1.22–2.25; P=0.001), peripheral vascular disease (OR =3.84; 95% CI: 1.66–8.85; P=0.002), renal disease (OR =3.30; 95% CI: 1.88–5.80; P<0.001), and severe pulmonary hypertension (OR =1.76; 95% CI: 1.13–2.72; P=0.01) were associated with an increased risk of VAP after cardiac surgery, whereas the risk of VAP was not affected by gender (OR =0.97; 95% CI: 0.72–1.33;

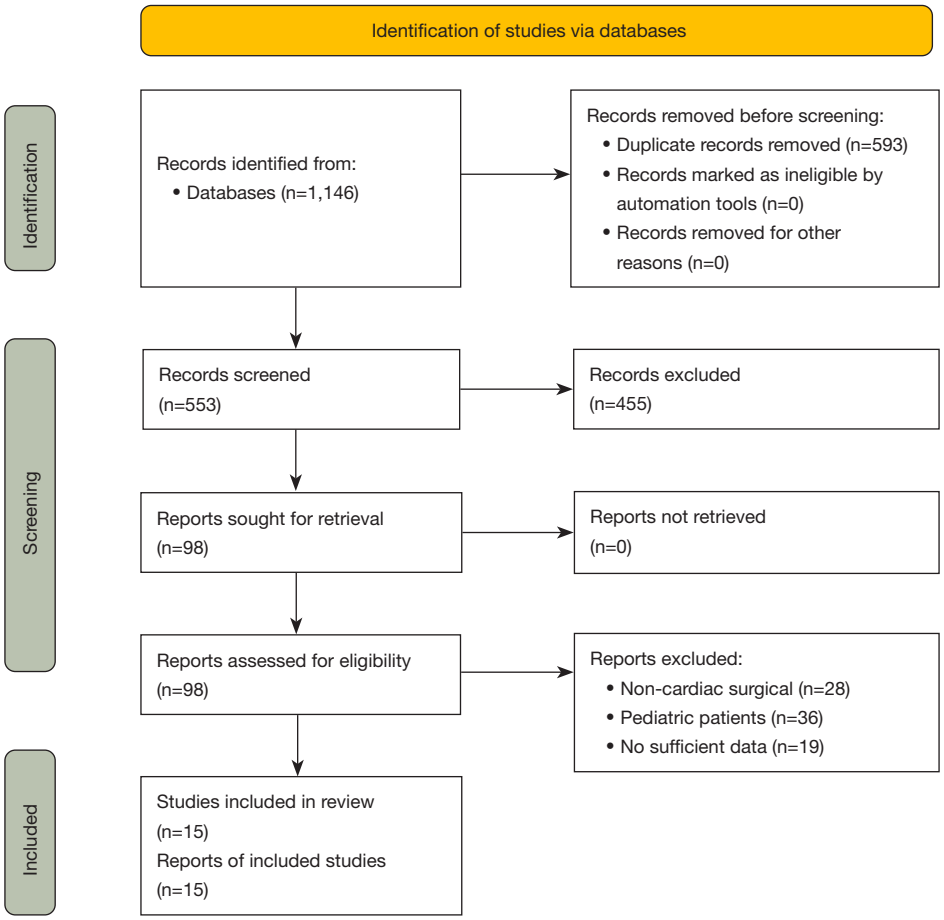

Figure 1 The Preferred Reporting Items for Systematic reviews and Meta-Analyses flowchart for literature search and study selection.

P=0.87), smoking (OR =1.56; 95% CI: 0.62–3.92; P=0.34), obesity (OR =0.89; 95% CI: 0.14–5.80; P=0.91), diabetes (OR =1.16; 95% CI: 0.94–1.44; P=0.17), hypertension (OR =0.89; 95% CI: 0.35–2.29; P=0.82), congestive heart failure (OR =5.86; 95% CI: 0.99–34.71; P=0.051), and neoplasia (OR =19.46; 95% CI: 0.53–708.46; P=0.11). There were potential significant heterogeneities across the included studies in terms of smoking (I^2=50.8%; P=0.15), obesity (I^2=90.9%; P=0.001), hypertension (I^2=83.5%; P=0.002), congestive heart failure (I^2=94.4%; P<0.001), peripheral vascular disease (I^2=69.9%; P=0.02), renal disease (I^2=57.5%; P=0.052), and neoplasia (I^2=83.2%; P=0.02). Furthermore, no significant heterogeneity was observed among the included studies in terms of age >70 years, sex, diabetes, COPD, or severe pulmonary hypertension.

Perioperative risk factors for VAP

A summary of the perioperative risk factors for VAP after cardiac surgery is shown in *Figure 4*. We noted emergency surgery (OR =6.41; 95% CI: 2.63–15.60; P<0.001), redo surgery (OR =3.38; 95% CI: 2.16–5.30; P<0.001), airway instrumentation (OR =2.77; 95% CI: 1.63–4.72; P<0.001), gastric aspiration (OR =4.30; 95% CI: 2.87–6.44; P<0.001), reintubation (OR =11.13; 95% CI: 5.56–22.26; P<0.001), mechanical ventilation duration >3 days (OR =3.70; 95% CI: 2.11–6.47; P<0.001), intra-aortic balloon (OR =5.27; 95% CI: 2.56–10.83; P<0.001), New York Heart Association >3 (OR =2.84; 95% CI: 1.81–4.46; P<0.001), American Society of Anesthesiologists >3 (OR =2.77; 95% CI: 1.68–4.55; P<0.001), need for transfusion during surgery (OR =9.25; 95% CI: 1.35–63.16; P=0.02), and

Table 1 The baseline characteristics of included studies and involved patients

Study	Region	Study design	Sample size [VAP]	Age (years)	Male (%)	Duration of MV (days)	VAP definition	Adjusted level	NOS scale
Torres 1990 (17)	Spain	Prospective	322 [78]	54.4	67.4	NA	Own description	Fully	8
Kollef 1993 (18)	USA	Prospective	102 [22]	NA	NA	NA	American College of Chest Physicians	Crude	6
Kollef 1995 (19)	USA	Prospective	107 [26]	NA	59.8	NA	American College of Chest Physicians	Crude	6
Kollef 1997 (20)	USA	Prospective	605 [59]	64.0	65.6	NA	CDC	Fully	7
Pawar 2003 (21)	India	Prospective	952 [25]	56.6	88.1	0.9	Own description	Fully	7
Bouza 2003 (22)	Spain	Prospective	356 [52]	64.1	62.6	1.1	CDC	Fully	8
Bouza 2006 (23)	Spain	Cross-sectional	321 [24]	NA	NA	NA	Spain	Crude	6
Hortal 2009 (24)	8 countries in Europe	Prospective	971 [20]	64.1	71.1	1.0	CDC	Fully	8
Hortal 2009 (25)	Spain	Prospective	1,844 [106]	64.7	57.4	1.1	CDC	Fully	8
Sheng 2012 (26)	China	Retrospective	1,688 [105]	54.0	56.1	1.3	American Thoracic Society	Fully	7
Tamayo 2012 (27)	Spain	Prospective	1,610 [124]	67.9	39.1	1.9	CDC	Crude	7
Jiao 2015 (28)	China	Prospective	92 [33]	48.1	51.1	4.1	CDC	Crude	6
Hassoun-Kheir 2020 (29)	Israel	Case-control	946 [57]	68.6	62.1	NA	American Thoracic Society	Crude	7
Macedo 2023 (30)	Brazil	Retrospective	472 [10]	62.3	72.0	NA	CDC	Crude	6
Song 2024 (31)	China	Case-control	90 [45]	47.8	54.4	3.1	CDC	Crude	6

VAP, ventilator-associated pneumonia; MV, mechanical ventilation; NOS, Newcastle-Ottawa Scale; CDC, Centers for Disease Control and Prevention; NA, not applicable.

ascending aortic surgery (OR =3.35; 95% CI: 1.13–9.94; P=0.03) were associated with an increased risk of VAP after cardiac surgery. However, prior surgery (OR =1.38; 95% CI: 0.80–2.40; P=0.25), coma (OR =10.73; 95% CI: 0.21–549.94; P=0.24), and tracheostomy (OR =40.22; 95% CI: 0.09–17,906.85; P=0.24) were not associated with the risk of VAP. There were significant heterogeneities among included studies for prior surgery (I^2=58.7%; P=0.046), emergency surgery (I^2=72.2%; P=0.01), coma (I^2=83.3%; P=0.02), tracheostomy (I^2=94.1%; P<0.001), reintubation (I^2=83.1%; P<0.001), mechanical ventilation duration >3 days (I^2=99.1%; P<0.001), intra-aortic balloon (I^2=67.3%; P=0.03), and need for transfusion during surgery (I^2=94.2%; P<0.001). Furthermore, no evidence of heterogeneity was observed for repeat surgery, airway instrumentation, gastric aspiration, New York Heart Association score >3, American Society of Anesthesiologists score >3, or ascending aortic surgery. Finally, we noted the length of cardiopulmonary bypass in VAP patients was significantly longer than non-VAP patients (WMD: 25.49 min; 95% CI: 21.97 to 29.01; P<0.001; *Figure 5*).

Publication bias

Publication bias for the incidence of VAP after cardiac surgery was also assessed, and a significant publication bias was observed (P value for Egger: <0.001; P value for Begg: 0.001; *Figure 6*). The conclusions did not change after adjusting for publication bias using the trim-and-fill method (32).

Discussion

This systematic review and meta-analysis was based on published articles and explored the incidence of and potential risk factors for VAP after cardiac surgery. A total

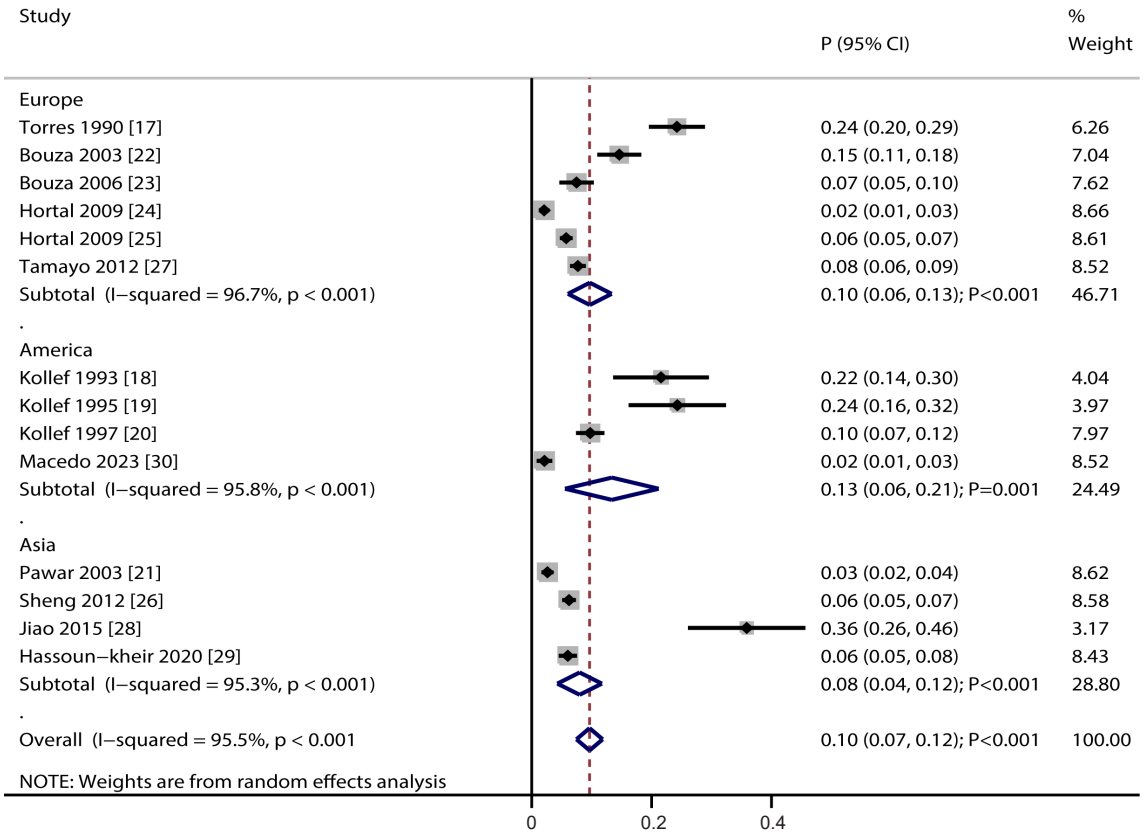

Figure 2 The pooled incidence of ventilator-associated pneumonia after cardiac surgery. CI, confidence interval.

of 10,478 patients who underwent cardiac surgery from 15 studies were included, and the characteristics of the patients varied widely. This study reported the pooled incidence of VAP after cardiac surgery, and found it was highest in America and lowest in Asia. Moreover, the preoperative and perioperative risk factors for VAP after cardiac surgery were also identified, thus clinical efforts should be applied in order to prevent the development of VAP for address modifiable risk factors.

Our study found that the prevalence of VAP after cardiac surgery was 10%, which was higher than that reported in a previous meta-analysis of nine studies (6). This study found that the prevalence of VAP ranged from 2% to 36%. Two of the included studies conducted in eight countries in Europe and Brazil reported an incidence of VAP of 2% (24,30). Moreover, a prospective study conducted by Jiao *et al.* reported the incidence of VAP to be 36%; which could be explained by the fact that this study included patients who received ≥48 h of mechanical ventilation, which was associated with a higher incidence of VAP (28). Furthermore, although the prevalence of VAP varied across the included studies, this may be because of the number of risk factors and comorbidities of the included patients. Finally, the incidence of VAP in Asia was lower than in Europe and America, which could be explained by the differences between Asian and Western countries in culture, nursing practices, population structure, genetic backgrounds, disease burdens, and postoperative patient follow-up.

Our study found that preoperative risk factors for VAP included age >70 years, COPD, peripheral vascular disease, renal disease, and severe pulmonary hypertension. Several reasons could explain these results: (I) as age increases, respiratory function gradually declines, respiratory muscles atrophy, lung elasticity decreases, and the ability to clear phlegm decreases (33); (II) immunosuppression in COPD is significantly associated with pulmonary infections, while prolonged endotracheal mechanical ventilation also increases the risk of VAP (34); (III) peripheral vascular disease is considered a significant risk factor for

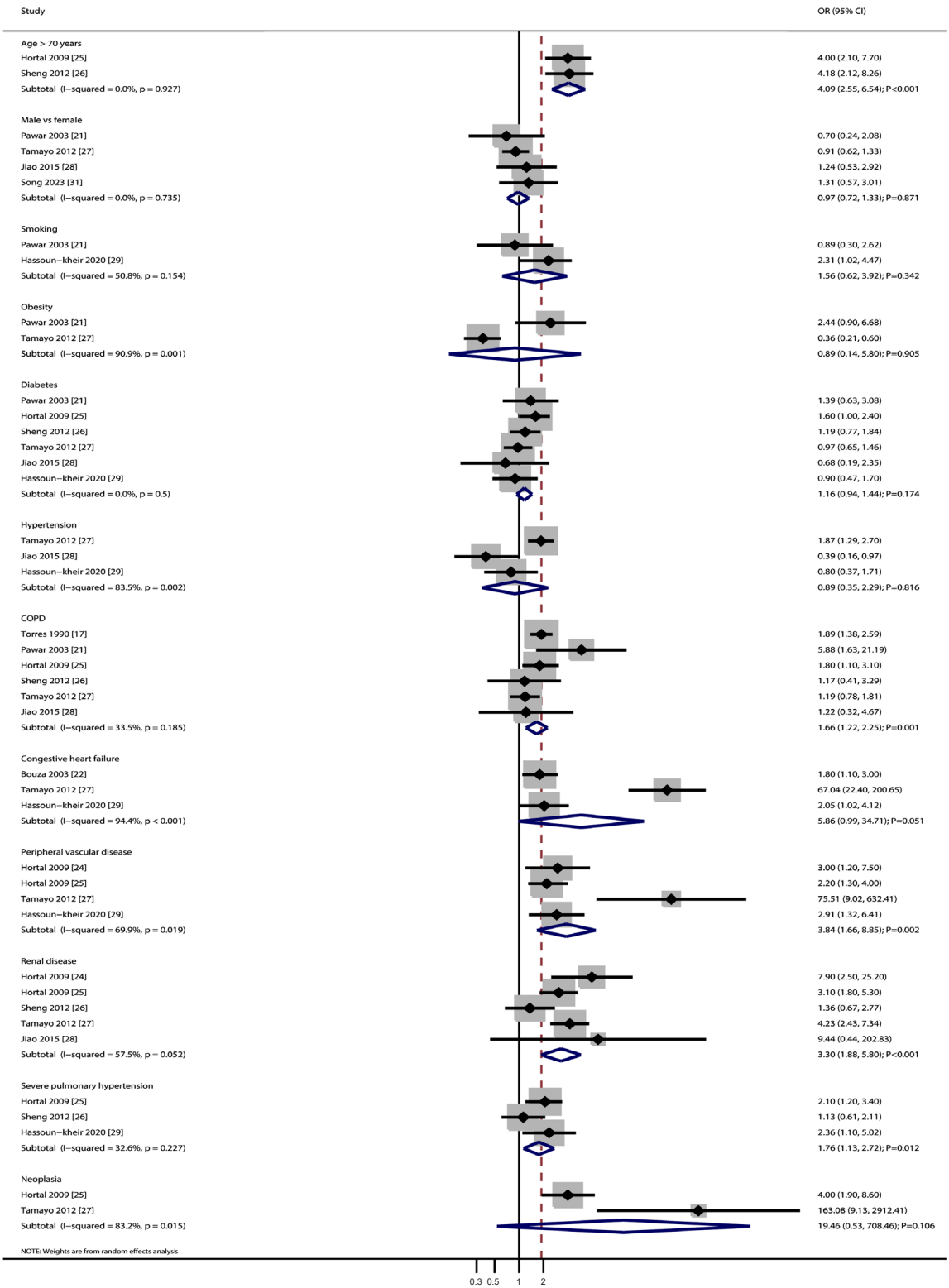

Figure 3 The preoperative risk factors for ventilator-associated pneumonia after cardiac surgery, including age, sex, smoking, obesity, diabetes, hypertension, COPD, congestive heart failure, peripheral vascular disease, renal disease, severe pulmonary hypertension, and neoplasia. OR, odds ratio; CI, confidence interval; COPD, chronic obstructive pulmonary disease.

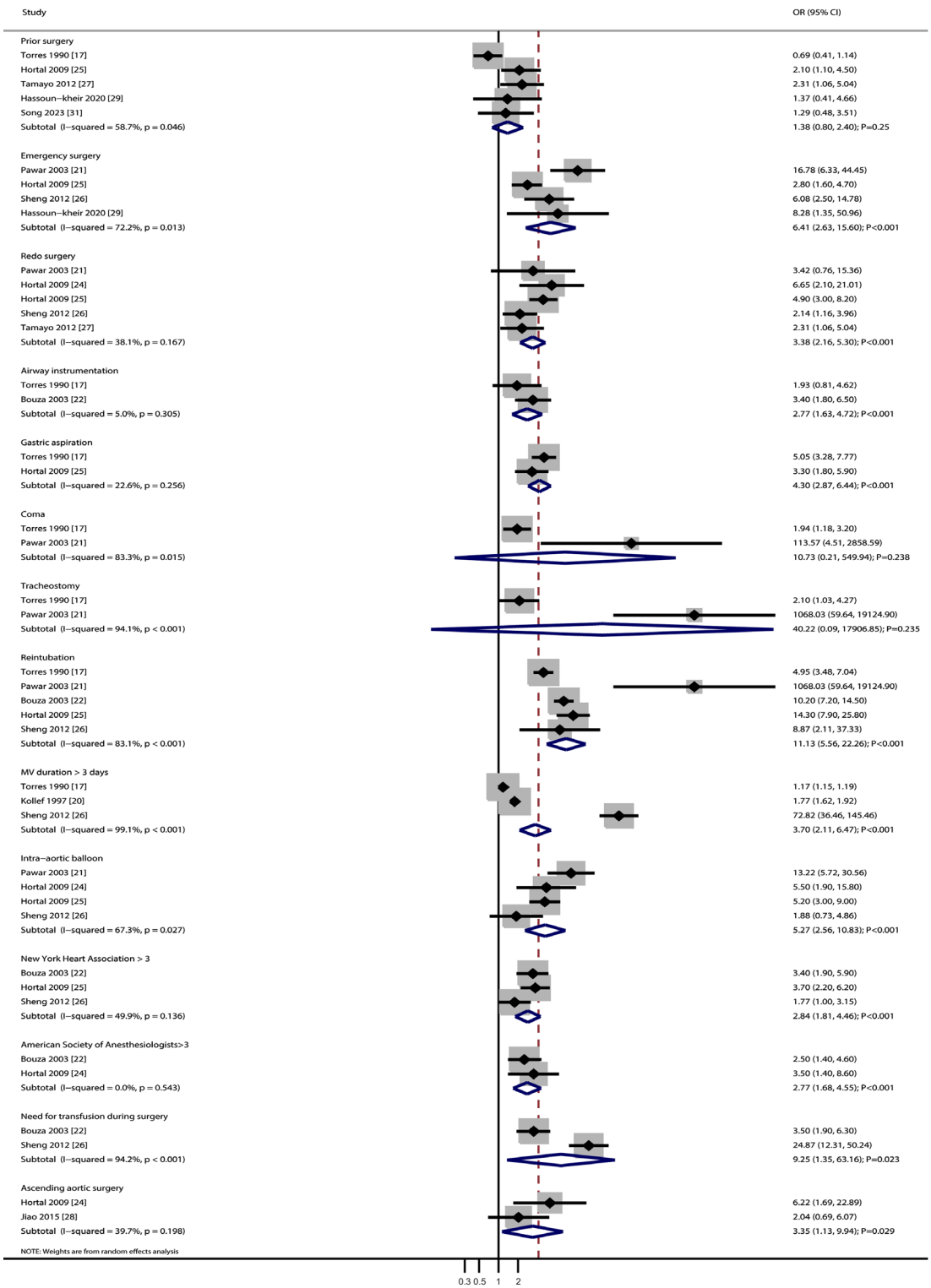

Figure 4 The perioperative risk factors for ventilator-associated pneumonia after cardiac surgery, including prior surgery, emergency surgery, redo surgery, airway instrumentation, gastric aspiration, coma, tracheostomy, reintubation, MV duration, intra-aortic balloon, New York Heart Association, American Society of Anesthesiologists, need for transfusion during surgery, and ascending aortic surgery. OR, odds ratio; CI, confidence interval; MV, mechanical ventilation.

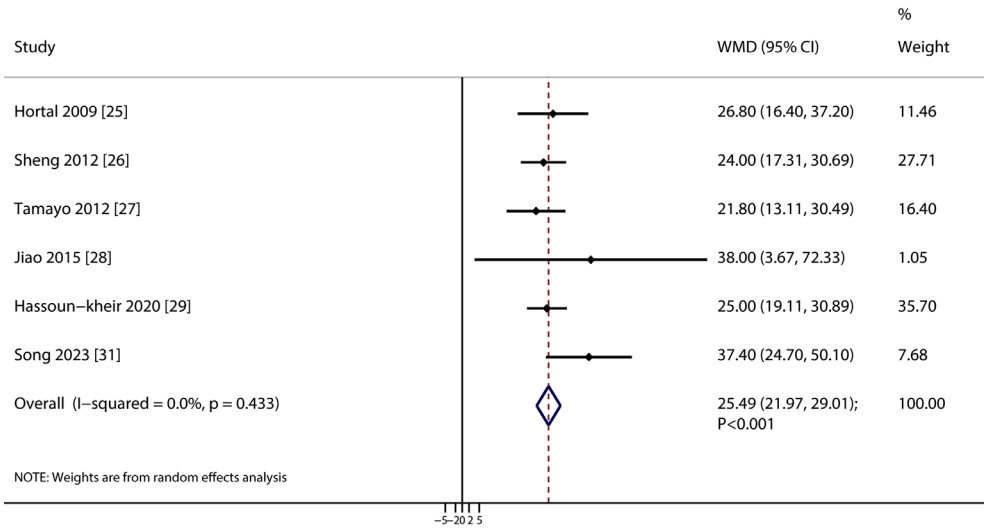

Figure 5 The length of cardiopulmonary bypass between ventilator-associated pneumonia patients and non-ventilator-associated pneumonia patients. WMD, weighted mean difference; CI, confidence interval.

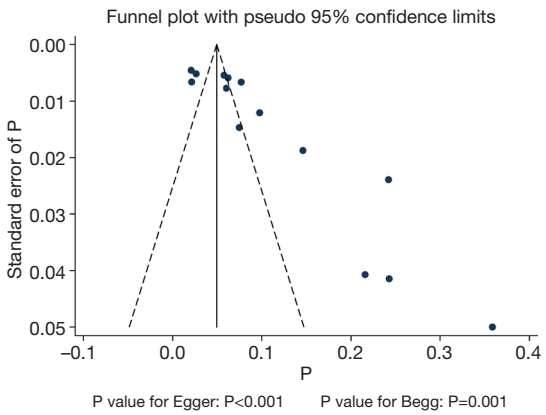

Figure 6 Funnel plot for the incidence of ventilator-associated pneumonia after cardiac surgery.

postoperative infection in patients undergoing cardiac surgery, which might affect the progression of VAP (35); (IV) poor renal function is associated with an increased risk of infection (36); and (V) pulmonary arterial hypertension can lead to pulmonary congestion, which can cause recurrent respiratory tract infections and pneumonia (37). Therefore, for patients aged over 70 years, those with COPD, peripheral vascular disease, renal disease, or severe pulmonary hypertension, perioperative management should be intensified to prevent the onset and progression of VAP.

The perioperative risk factors for VAP after cardiac surgery included emergency surgery, redo surgery, airway instrumentation, gastric aspiration, reintubation, mechanical ventilation duration >3 days, intra-aortic balloon, New York Heart Association score >3, American Society of Anesthesiologists score >3, the need for transfusion during surgery, and ascending aortic surgery. Cardiac surgery, particularly cardiopulmonary bypass surgery, often triggers abnormal systemic inflammatory responses, leading to the release of numerous proinflammatory mediators. Additionally, considering other factors, such as anesthesia and hypothermia, postoperative lung dysfunction is common in patients requiring long-term mechanical ventilation. The longer the duration of mechanical ventilation, the higher the risk of VAP (38-40). Furthermore, perioperative risk factors are often associated with disease severity, which significantly increases the incidence of VAP. Cardiopulmonary bypass induces a certain degree of systemic inflammatory response and immune suppression, weakening the body's ability to fight infections and thereby increasing the risk of pulmonary infections. Moreover, patients often require deep sedation or muscle relaxation, which hampers the natural clearance of airway secretions, allowing accumulated secretions to provide a breeding ground for bacteria. Lastly, contact between blood and non-biological surfaces during cardiopulmonary bypass can activate the complement and coagulation systems, generating inflammatory mediators that exacerbate the pulmonary inflammatory state, further compromising its ability to resist infections (2,41). Patients should be stratified into risk categories based on

intraoperative risk factors for VAP, with early interventions targeted at high-risk individuals to prevent the occurrence of VAP.

There are some limitations in this study. First, the analysis was based on cross-sectional, prospective, and retrospective observational studies, and the conclusions may have been biased owing to uncontrolled confounding factors. Second, the type of cardiac surgery, such as minimally invasive approach, differed across the included studies and was significantly related to perioperative factors, thus affecting the risk of VAP. Third, the definition of VAP differed among the included studies, which may have affected the net effect estimate. Finally, the inherent limitations of the meta-analysis were based on published articles, including inevitable publication bias and restricted detailed analysis.

Conclusions

This study found that the incidence of VAP after cardiac surgery was 10%, which was the highest in America and lowest in Asia. Moreover, comprehensive risk factors, including preoperative and perioperative risk factors for VAP after cardiac surgery, were explored. Given previous study suggesting that the systematic use of computed tomography (CT) scans prior to cardiac surgery can reduce unnecessary surgeries, it is conceivable that genomic imaging data may also hold potential value in predicting VAP (42). Therefore, patients undergoing heart surgery should have a predictive model for VAP based on identified risk factors and genomic imaging data, and early intervention should be implemented to improve the prognosis of patients with VAP.

Acknowledgments

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Footnote

Reporting Checklist: The authors have completed the PRISMA reporting checklist. Available at https://jtd.amegroups.com/article/view/10.21037/jtd-24-324/rc

Peer Review File: Available at https://jtd.amegroups.com/article/view/10.21037/jtd-24-324/prf

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://jtd.amegroups.com/article/view/10.21037/jtd-24-324/coif). The authors have no conflicts of interest to declare.

Ethical Statement: 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.

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