

Efficacy and safety of noninvasive ventilation in patients after cardiothoracic surgery

A PRISMA-compliant systematic review and meta-analysis

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Abstract

Background: Noninvasive ventilation (NIV) is a promising therapeutic strategy after cardiothoracic surgery. This study aimed to meta-analyze the efficacy and safety of NIV as compared to conventional management after cardiothoracic surgery.

Methods: PubMed, EMBASE, and Cochrane Library databases were searched for randomized controlled trials (RCTs) comparing NIV with conventional management after cardiothoracic surgery. Relative risk (RR), standard mean difference (SMD), and 95% confidence intervals (CIs) were used to measure the efficacy and safety of NIV using random-effects model. Heterogeneity was evaluated using the Q statistic.

Results: This study included 14 RCTs (1740 patients) for the evaluation of efficacy and safety of NIV as compared to conventional management after cardiothoracic surgery. Overall, NIV had minimal effect on the risk of mortality (RR: 0.64; 95% CI: 0.36–1.14; $P=0.127$), endotracheal intubation (RR: 0.52; 95% CI: 0.24–1.11; $P=0.090$), respiratory (RR: 0.70; 95% CI: 0.47–1.30; $P=0.340$), cardiovascular (RR: 0.81; 95% CI: 0.54–1.22; $P=0.306$), renal (RR: 0.70; 95% CI: 0.26–1.92; $P=0.491$), and other complications (RR: 0.72; 95% CI: 0.38–1.36; $P=0.305$), respiratory rate (SMD: -0.10 ; 95% CI: -1.21 – 1.01 ; $P=0.862$), heart rate (SMD: -0.27 ; 95% CI: -0.76 – 0.22 ; $P=0.288$), PaO₂/FiO₂ ratio (SMD: -0.34 ; 95% CI: -0.17 – 0.85 ; $P=0.194$), PaCO₂ (SMD: 0.83; 95% CI: -0.12 – 1.77 ; $P=0.087$), systolic pressure (SMD: -0.04 ; 95% CI: -0.25 – 0.17 ; $P=0.700$), pH (SMD: -0.01 ; 95% CI: -0.44 – 0.43 ; $P=0.974$), length of ICU stay (SMD: -0.19 ; 95% CI: -0.47 – 0.08 ; $P=0.171$), and hospital stay (SMD: -0.31 ; 95% CI: -1.00 – 0.38 ; $P=0.373$). Sensitivity analysis showed that NIV was associated with higher levels of PaO₂/FiO₂ ratio (SMD: 0.52; 95% CI: 0.00–1.05; $P=0.048$) and lower risk of endotracheal intubation (RR: 0.38; 95% CI: 0.22–0.66; $P=0.001$).

Conclusion: As compared to conventional management, the use of NIV after cardiothoracic surgery improved patient's oxygenation and decreased the need for endotracheal intubation, without significant complications.

Abbreviations: CI = confidence interval, COPD = chronic obstructive pulmonary disease, NIV = noninvasive ventilation, RR = relative risk, SMD = standard mean difference.

Keywords: meta-analysis, NIV, surgery, systematic review

1. Introduction

Although postoperative mortality and adverse effects after cardiac or thoracic vascular surgery have decreased due to advances in modern surgery, the safety remains a significant concern.^[1] Deterioration of pulmonary function is a frequent postoperative

complication and remains a significant cause of postoperative mortality.^[2–4] Impaired pulmonary oxygen transfer is primarily attributed to a decrease in functional residual capacity in about 70% of patients following thoracotomy.^[5] Postoperative hypoxemia is associated with increased risk of nosocomial pulmonary infections, contributing to postoperative morbidity and mortality.^[6,7]

Noninvasive ventilation (NIV) is widely used in patients with acute exacerbations of chronic obstructive pulmonary disease (COPD), cardiogenic pulmonary edema, and hypoxemic respiratory failure.^[8] Studies suggested that NIV was associated with a lower risk of acute respiratory failure after cardiac or thoracic surgery.^[9] As compared to invasive ventilation, patients undergoing NIV require lower sedation, which improves comfort level and reduces the risk of ventilator-associated pneumonia.^[10] Further, NIV improves gas exchange, decreases breathing distress, and reduces atelectasis in patients after cardiac or thoracic surgery, which in turn reduces the need for reintubation and improves clinical outcomes.^[11]

In previous meta-analyses,^[12] out-of-hospital administration of NIV was associated with a reduced risk of hospital mortality and the need for invasive ventilation. Insufficient evidence is available to support the use of routine NIV in patients with stable COPD.^[13] However, the role of NIV in patients after cardiac or thoracic surgery remains controversial. The present meta-analysis was designed to elucidate the efficacy and safety of NIV, and enable physicians to select the appropriate interventions after cardiac or thoracic surgery.

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2. Materials and methods

2.1. Data sources, search strategy, and selection criteria

This review was conducted and reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis Statement issued in 2009.^[14] Ethics approval was not necessary for this study, as only deidentified pooled data from individual studies were analyzed.

PubMed, EMBASE, and Cochrane library databases were searched for articles published since the beginning of NIV use up to April 2015, using the keywords:

“Noninvasive mechanical ventilation OR Noninvasive positive pressure ventilation OR NPPV OR continuous positive pressure ventilation OR noninvasive continuous positive airway pressure OR noninvasive positive pressure ventilation OR early nasal high flow oxygen therapy” AND “cardiac surgery OR thoracic surgery OR lung resection surgery OR pulmonary resection OR esophagectomy” AND “pulmonary complications OR acute respiratory distress syndrome OR acute respiratory failure OR respiratory complications” and were filtered with “Randomized Controlled Trial.” The search had no restrictions on language or publication status (published or in press). We also conducted a manual search of reference lists from all retrieved articles and relevant review articles. The medical subject heading, methods, patients’ status, study design, interventions, and reported outcomes of potential articles were used to identify the relevant trials.

The study retrieval was independently performed by 2 reviewers. Any inconsistencies between the 2 reviewers were settled by group discussion until a consensus was reached. Inclusion criteria were: randomized controlled trial (RCT) design; investigation of the efficacy and safety of NIV versus conventional management in patients after cardiac or thoracic surgery; and reporting at least one of the following outcomes: mortality, endotracheal intubation, respiratory, cardiovascular, renal and other complications, respiratory rate, heart rate, PaO₂/FiO₂ ratio, PaCO₂, systolic pressure, pH, length of intensive care unit (ICU) stay, and length of hospital stay.

2.2. Data collection and quality assessment

Data abstraction and assessment were independently performed by 2 reviewers using a standardized approach. Publication data were extracted as follows: first author name, country, sample size, mean age, gender, patients’ status, interventions, control, and reported outcomes. Any disagreement was resolved by discussion with a 3rd reviewer.

Two reviewers independently evaluated the quality of trials using Jadad guidelines.^[15] The Jadad scale assesses the reporting of essential features in n RCT, that is, randomization, blinding, withdrawals, and dropouts. The 3-point questionnaire generates a total score ranging from 0 (worst) to 5 (best).^[15] In case of disagreement, a consensus was reached after discussion.

2.3. Statistical analysis

Relative risks (RRs) or standard mean differences (SMDs) with 95% confidence intervals (CIs) were calculated using outcomes extracted from each study before data pooling. We used RRs with 95% CIs to estimate the safety of NIV versus conventional management for mortality, endotracheal intubation, respiratory, cardiovascular, renal, and other complications. We used SMDs with 95% CI to estimate the efficacy of NIV versus conventional

management for respiratory heart rates, PaO₂/FiO₂ ratio, PaCO₂, systolic pressure, pH, length of ICU stay, and length of hospital stay.^[16]

Heterogeneity among trials was investigated using the *Q* statistic. *P* < 0.10 was indicative of significant heterogeneity.^[17] Subgroup analyses were conducted to explore potential sources of heterogeneity on the basis of disease status. Sensitivity analysis was conducted to assess the impact of individual trials on higher heterogeneity based on the results of meta-analysis.^[18] The Egger^[19] and Begg tests^[20] were used to statistically evaluate publication bias. All reported *P* values were 2-sided, and *P* values < 0.05 were considered statistically significant for all included studies. Statistical analyses were performed using STATA software (version 10.0; Stata Corporation, College Station, TX).

3. Results

The study selection process is outlined in Fig. 1. Eight to nine potentially relevant references were identified after a systematic search of electronic databases, professional journals, and other sources. After reviewing the title or abstract, 48 references were excluded, leaving 41 articles for full-text review. Eight studies were discarded at the stage of full-text review. Among the remaining 33 citations, 14 studies^[21–34] were finally identified and included in the analysis of efficacy and safety of NIV versus conventional management in patients after cardiac or thoracic surgery. Studies were excluded for the following reasons: conference abstracts without full-text, incomparable data, and irrelevance. A manual search of the reference lists of these trials did not yield any new eligible studies. The general characteristics of the included studies are presented in Table 1. The sample sizes of each trial varied from 25 to 360 patients. Ten studies were

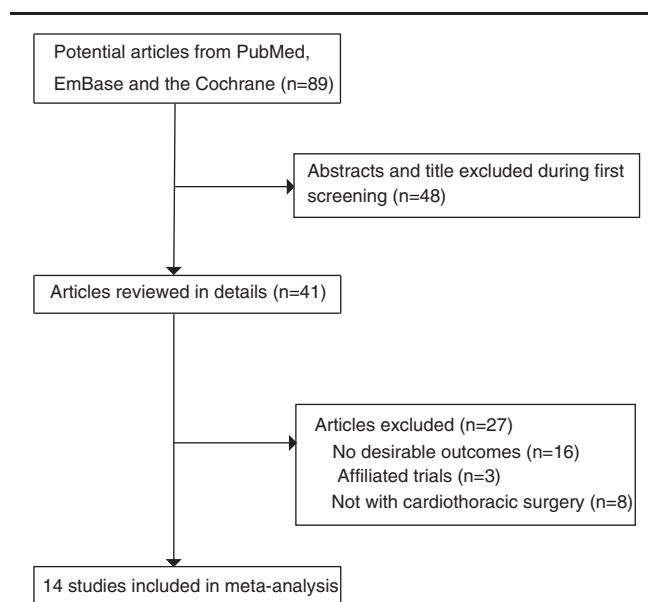


Figure 1. Study selection process. Eight to nine potentially relevant studies were identified after a systematic search of electronic databases, professional journals, and other sources. After reviewing the titles and abstracts, 48 were excluded for failure to meet the inclusion criteria. Eight studies were excluded at the stage of full-text review. Among the remaining 33 studies, 14 were related to efficacy and safety of noninvasive ventilation (NIV) versus conventional management in patients after cardiac or thoracic surgery.

Table 1

Baseline characteristics of studies included in the systematic review and meta-analysis.

Study	Country	Sample size	Mean age	Gender (M/F)	Status of patients	Intervention	Control	Reported outcomes	Jadad scale
Al-Mutairi et al ^[21]	Saudi Arabia	72/36	62.0	98/10	Cardiac surgery	CPAP therapy every 2 hours, CPAP therapy every 4 hours	Incentive spirometry	Mortality	2
Al Jaaly et al ^[22]	United Kingdom	63/63	65.8/69.4	NA	Cardiopulmonary bypass and mild hypothermia	BIPAP during the first 24 hours after extubation	Conventional management	PaCO ₂ ; mortality; adverse events	1
Auriant et al ^[23]	France	24/24	63.0/58.9	NA	Lung resection	NPV and exhaled tidal volume of 8 to 10 mL/kg and a respiratory rate of less than 25 breaths/minute	Oxygen supplementation, SaO ₂ above 90%, PCA, chest physiotherapy	Mortality; length of ICU stay; length of hospital stay; endotracheal mechanical ventilation; heart rate; respiratory rate; PaO ₂ /FIO ₂ ratio; PaCO ₂ ; pH; systolic pressure	3
Barbagallo et al ^[24]	Italy	25/25	65.0/69.0	35/15	Pulmonary lobectomy	Heimat CPAP: 2 CPAP cycles of 2 hours	Short-term antibiotic prophylaxis 3 times a day, chest physiotherapy once daily	PaO ₂ /FIO ₂ ratio; mortality	2
Böhner et al ^[25]	Germany	99/105	64.1/64.5	166/38	Major vascular surgery	nCPAP: a high-flow gas source (>50 l/minute)	Oxygen was administered at ambient pressure via a non-occlusive face mask	Mortality; PaCO ₂ ; endotracheal mechanical ventilation; PaO ₂ /FIO ₂ ratio; length of ICU stay; length of hospital stay; systolic pressure; adverse events	3
Fagøvik Olsen et al ^[26]	Sweden	34/36	62.0/64.1	60/10	Thoraco-abdominal resection	CPAP 30minutes every 2 hours	IR-PEP; 30 deep breaths with; huffing and cough between every tenth breath at 2-hour; intervals	Mortality; length of ICU stay; length of hospital stay; endotracheal mechanical ventilation	3
Garutti et al ^[27]	Spain	55/55	62.1/63.1	65/45	Lung resection	CPAP via a Boussignac facial mask during the first 6 hours after surgery improved oxygenation at 24 hours	Venturi; supplemental; oxygen through venturi mask	PaO ₂ /FIO ₂ ratio; length of hospital stay; mortality; adverse events	3
Lorut et al ^[28]	France	181/179	63.6/63.7	276/84	Major lung resection	NIV applied intermittently 6 hours per day for 48 hours following surgery	Conventional postoperative treatment	Length of hospital stay; mortality; endotracheal mechanical ventilation; adverse events	3
Lucangelo et al ^[29]	Italy	22/22	68.5/61.0	35/9	Pulmonary resection	CPAP 20minutes OLV (CMV); 92.5 OLV (CMV Trial)	HPV 20 minutes OLV (CMV); 80 minutes OLV (CMV Trial)	PaCO ₂ ; heart rate; MAP; adverse events	2
Pasquina et al ^[30]	Switzerland	75/75	66.0/65.0	111/39	Cardiac surgery	CPAP 30-minute sessions four times a day	NIPSV 30-minute sessions four times a day	pH; PaCO ₂ ; PaO ₂ /FIO ₂ ratio; mortality	2
Pimila et al ^[31]	Canada	32/26	56.2/59.4	55/3	Elective aortocoronary bypass surgery	CPAP 12 hours by face mask and nose mask every 30 minutes for the first 2 hours	Supplemental oxygen via venti-mask after extubation	PaO ₂ /FIO ₂ ratio; length of ICU stay	1
Stock et al ^[32]	US	13/12	58.0/58.0	19/6	Cardiac operation	CPAP	All treatments lasted 15 minutes, were delivered every 2 hours during waking hours from the 2nd to the 72nd hours after extubation	PaCO ₂ ; pH	1
Zarbock et al ^[33]	Germany	146/146	66.0/64.0	206/86	Cardiac surgery coronary bypass surgery or heart valve replacement	nCPAP applied for at least 6 hours during the first 2 hours	oxygen, physiotherapy, intermittent; nCPAP for 10 minutes at 10 cm H ₂ O every 4 hours, and drug treatment	Length of ICU stay; length of hospital stay; adverse events	2
Zhu et al ^[34]	China	48/47	62.0/61.0	59/36	Cardiac surgery	NPV therapy using BiPAP S/P mode	Standard medical care and oxygen therapy	Mortality; endotracheal mechanical ventilation	3

BIPAP = bi-level positive airway pressure, CMV = conventional mechanical ventilation, ICU = intensive care unit, IR-PEP = inspiratory resistance-positive expiratory pressure, NA = not available, nCPAP = nasal continuous positive airway pressure, NIPSV = noninvasive pressure support ventilation, NPV = noninvasive positive pressure ventilation, OLV = open lung ventilation, PCA = patient controlled analgesia.

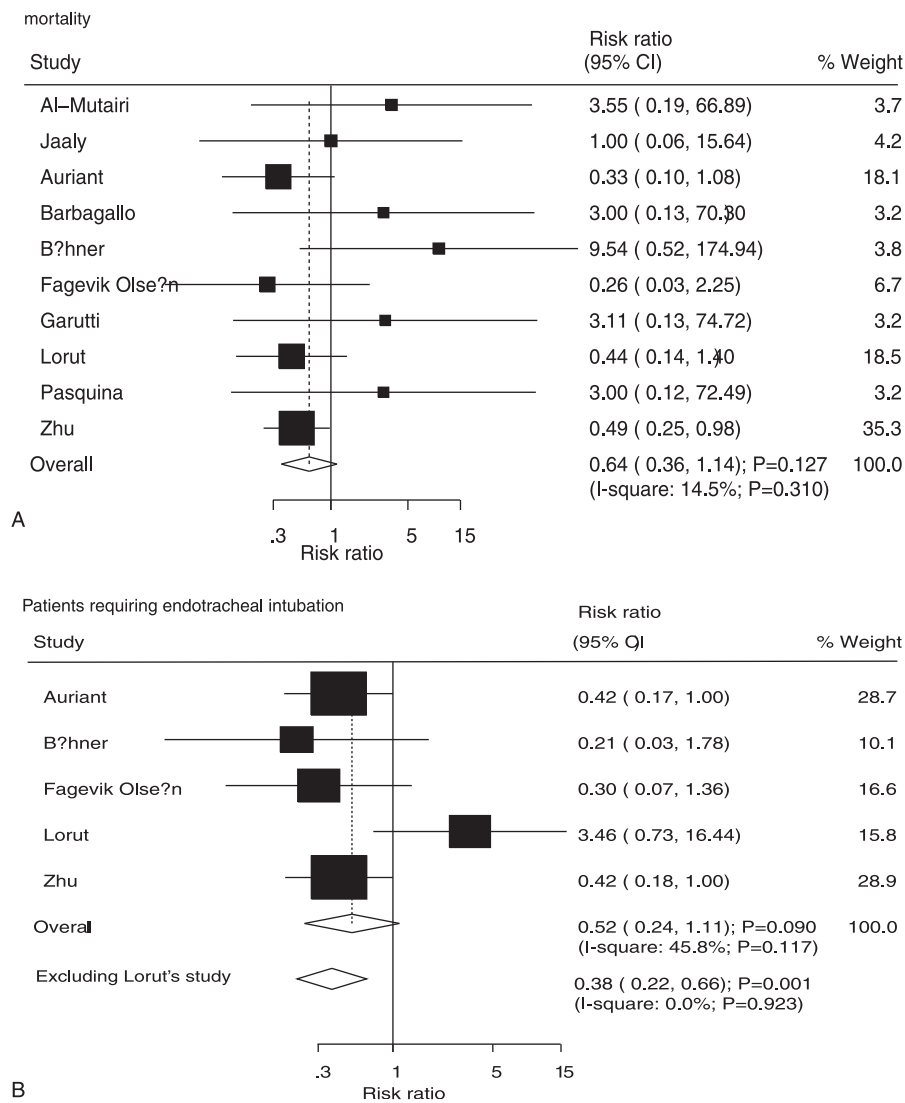


Figure 2. Association of noninvasive ventilation (NIV) with mortality and endotracheal intubation. (A) Lack of association of NIV with mortality; (B) lack of association of NIV with endotracheal intubation.

conducted in Europe,^[22–30,33] 2 in Asia,^[21,34] and the remaining 2 in America.^[31,32] The study quality of these 14 trials was evaluated using Jadad scale. A study with a score ≥ 3 represented high quality. Overall, 6 studies had a score of 3,^[23,25–28,34] 5 studies had a score of 2,^[21,24,29,30,33] and the remaining 3 studies had a score of 1.^[22,31,32]

The summary RR showed that the use of NIV was not associated with mortality (RR: 0.64; 95% CI: 0.36–1.14; $P=0.127$; Fig. 2A) or the risk of endotracheal intubation (RR: 0.52; 95% CI: 0.24–1.11; $P=0.090$; Fig. 2B). Moderate heterogeneity was observed between the trials. According to the sensitivity study, after excluding Lorut study,^[28] patients undergoing NIV were associated with a significantly reduced risk of endotracheal intubation (RR: 0.38; 95% CI: 0.22–0.66; $P=0.001$; Fig. 2B).

NIV had no significant effect on the risk of respiratory (RR: 0.70; 95% CI: 0.47–1.30; $P=0.340$; Fig. 3A), cardiovascular (RR: 0.81; 95% CI: 0.54–1.22; $P=0.306$; Fig. 3B), renal (RR: 0.70; 95% CI: 0.26–1.92; $P=0.491$; Fig. 3C), and other complications (RR: 0.72; 95% CI: 0.38–1.36; $P=0.305$; Fig. 3D). Substantial heterogeneity was detected for respiratory

complications. Therefore, a sensitivity analysis was conducted for respiratory complications, and each study was sequentially excluded from the pooled analysis. The conclusion was not affected by the exclusion of specific studies.

The pooled analyses showed that NIV was not associated with respiratory rate (SMD: -0.10 ; 95% CI: -1.21 – 1.01 ; $P=0.862$; Fig. 4A), heart rate (SMD: -0.27 ; 95% CI: -0.76 – 0.22 ; $P=0.288$; Fig. 4B), $\text{PaO}_2/\text{FiO}_2$ ratio (SMD: 0.34 ; 95% CI: -0.17 – 0.85 ; $P=0.194$; Fig. 4C), PaCO_2 (SMD: 0.83 ; 95% CI: -0.12 – 1.77 ; $P=0.087$; Fig. 4D), systolic pressure (SMD: -0.04 ; 95% CI: -0.25 – 0.17 ; $P=0.700$; Fig. 5A), pH (SMD: -0.01 ; 95% CI: -0.44 – 0.43 ; $P=0.974$; Fig. 5B), length of ICU stay (SMD: -0.19 ; 95% CI: -0.47 – 0.08 ; $P=0.171$; Fig. 5C), and length of hospital stay (SMD: -0.31 ; 95% CI: -1.00 – 0.38 ; $P=0.373$; Fig. 5D). Substantial heterogeneity was detected in the above outcomes, except systolic pressure. We then conducted sensitivity analyses and found that after excluding Pasquina study,^[30] NIV was associated with higher $\text{PaO}_2/\text{FiO}_2$ ratio (SMD: 0.52 ; 95% CI: 0.00 – 1.05 ; $P=0.048$). For other outcomes, the results were not affected by the exclusion of any individual trial.

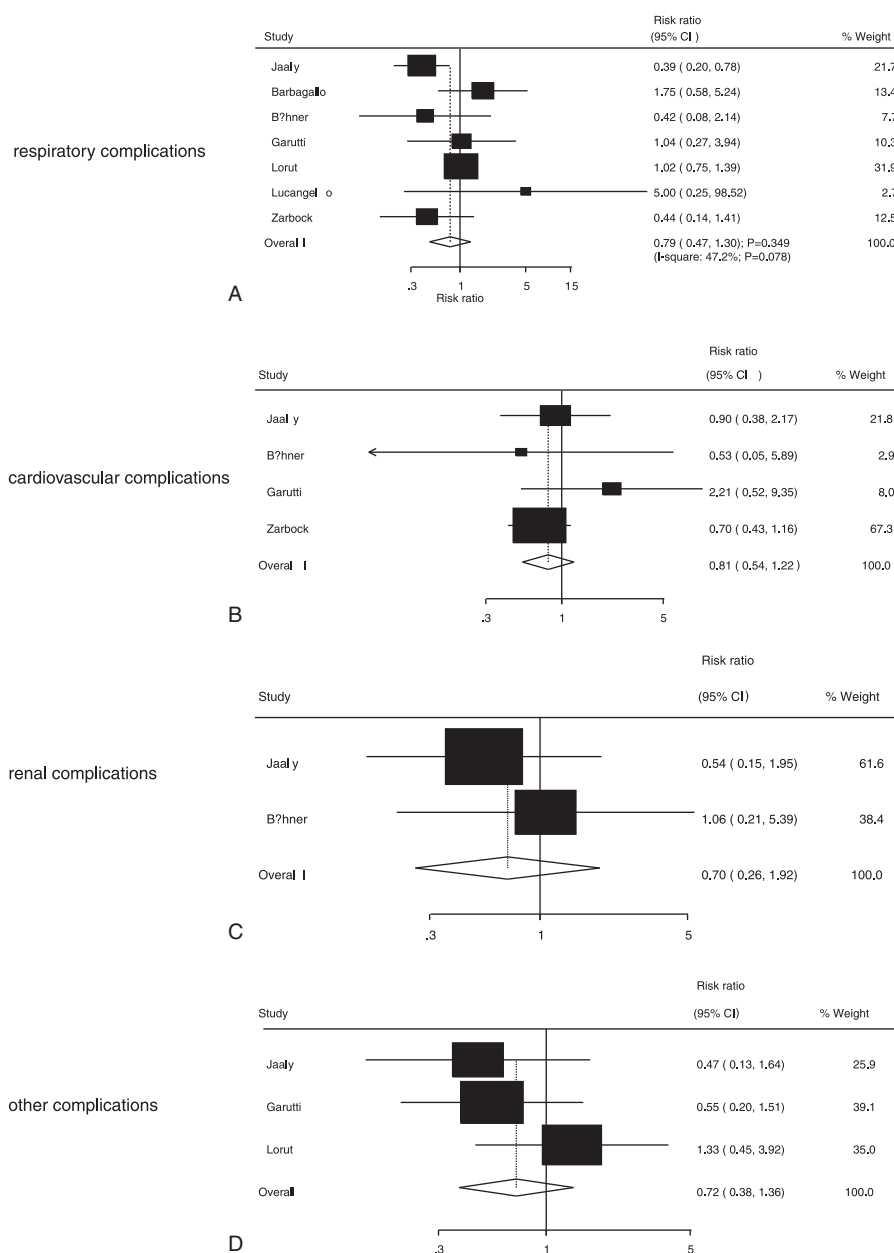


Figure 3. Association of noninvasive ventilation (NIV) with complications. Data suggest absence of any association between NIV and (A) respiratory complications, (B) cardiovascular complications, (C) renal complications, or (D) other complications.

We conducted subgroup analyses to minimize heterogeneity and evaluated the efficacy and safety of NIV in specific subpopulations (Table 2). Overall, NIV played an important role in determining patients' need for endotracheal intubation and respiratory complications, respiratory rate, and pH in patients undergoing cardiac surgery. Furthermore, NIV showed a significant effect on mortality, respiratory and heart rate, PaO₂/FiO₂ ratio, and pH in patients undergoing pulmonary surgery. No other significant effect was observed based on disease status.

The Egger^[19] and Begg test^[20] results showed no evidence of publication bias in the need for endotracheal intubation (*P* value for Egger: 0.762 and Begg: 0.462), respiratory (*P* value for Egger: 0.774 and Begg: 1.000), cardiovascular (*P* value for Egger: 0.529 and Begg: 0.734), and other complications (*P* value for Egger: 0.930 and Begg: 1.000), PaCO₂ (*P* value for Egger: 0.235 and

Begg: 0.133), PaO₂/FiO₂ ratio (*P* value for Egger: 0.062 and Begg: 0.133), pH (*P* value for Egger: 0.314 and Begg: 0.308), heart rate (*P* value for Egger: 0.290 and Begg: 1.000), systolic pressure (*P* value for Egger: 0.541 and Begg: 1.000), length of ICU stay (*P* value for Egger: 0.080 and Begg: 0.086), and length of hospital stay (*P* value for Egger: 0.892 and Begg: 1.000). Although the Begg test showed no evidence of publication bias for mortality (*P*=0.107), the Egger test revealed a bias (*P*=0.014). The conclusion was unchanged after adjustment for publication bias using the "trim and fill" method.^[35]

4. Discussion

The objective of the present meta-analysis was to determine the efficacy and safety of NIV use in patients after cardiac or thoracic

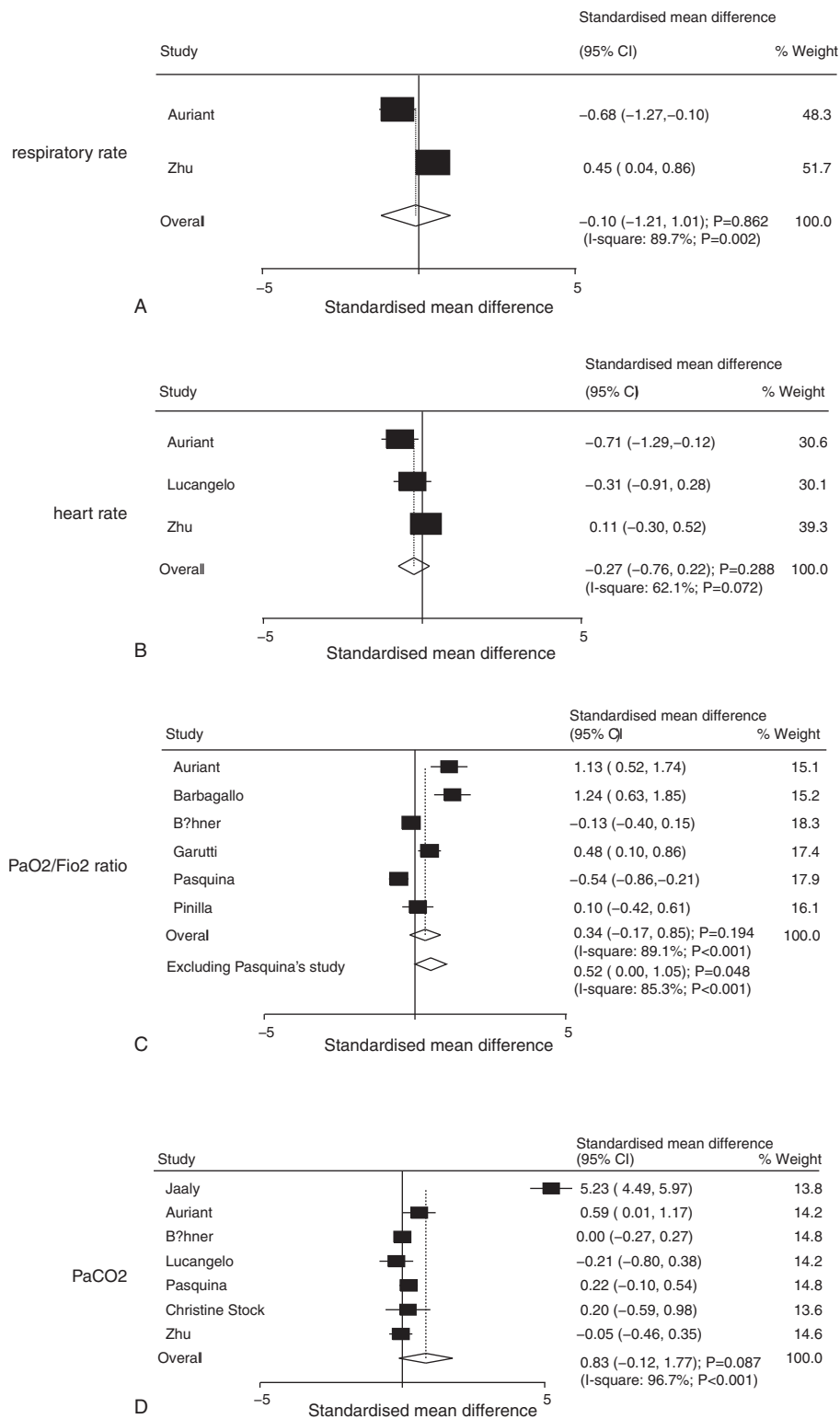


Figure 4. Pooled effect of noninvasive ventilation (NIV) on clinical indicators. (A) Respiratory rate, (B) heart rate, (C) PaO₂/Fio₂ ratio, and (D) PaCO₂.

surgery. Fourteen trials were identified, which included 1740 patients. We found that NIV had no significant effect in the treatment of patients after cardiothoracic surgery. However, the sensitivity results showed that NIV played an important role in PaO₂/Fio₂ ratio and endotracheal intubation, with no significant effect on the risk of other outcomes. Finally, subgroup analyses indicated that NIV

played an important role in multiple outcomes in patients with specific disease status. These results might help to better define the efficacy and safety of NIV in patients after cardiac or thoracic surgery, and enable the selection of appropriate treatment strategies.

The methodological evaluation of each included study was limited by randomization, blinding, withdrawals, and dropouts.

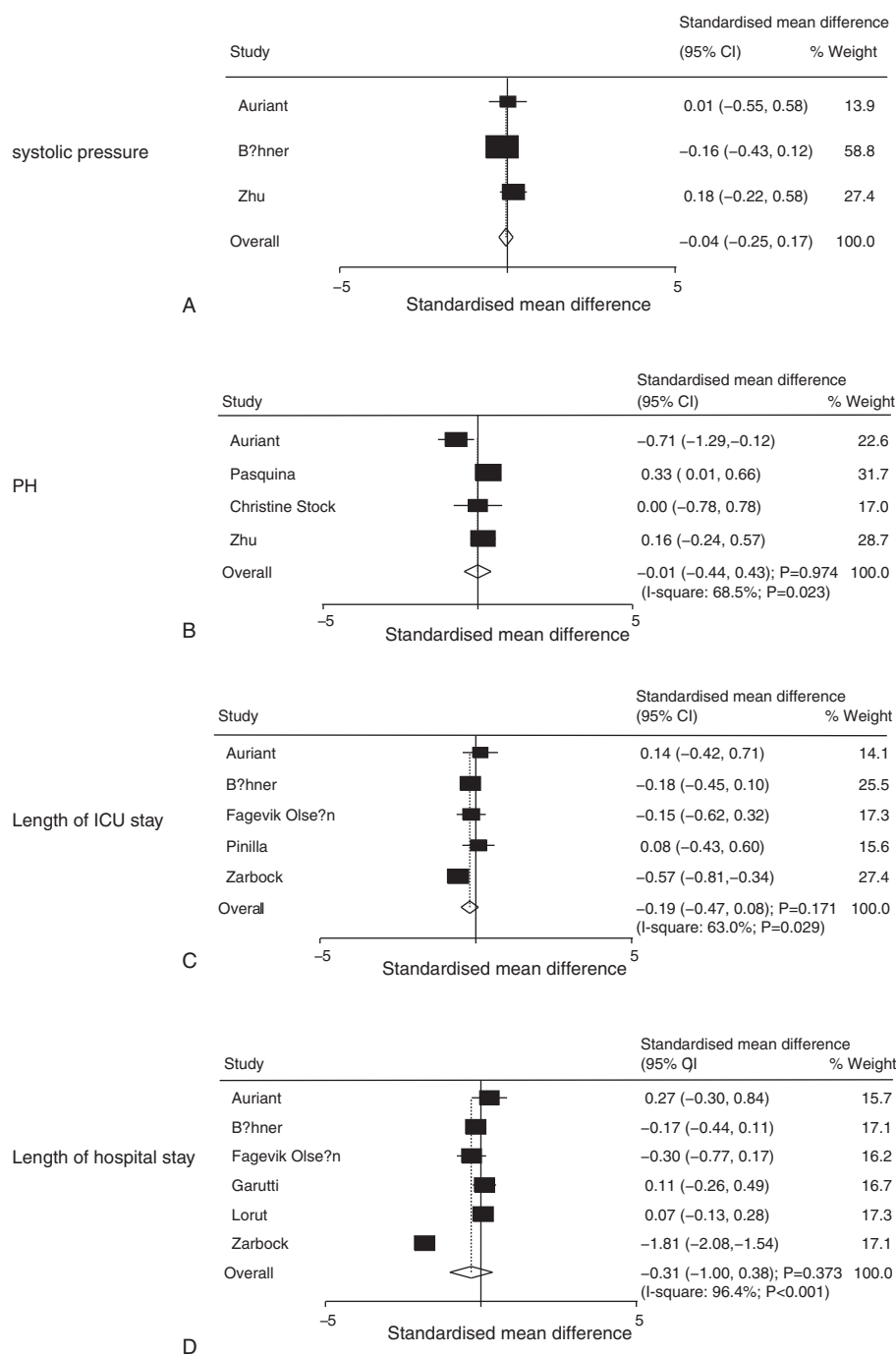


Figure 5. Pooled effect of NIV on hospital indicators. (A) Systolic pressure, (B) pH, (C) length of ICU stay, and (D) length of hospital stay. ICU=intensive care unit, NIV=noninvasive ventilation.

Although most trials reported withdrawals and dropouts, and use of intention-to-treat analysis, majority of the trials included in our meta-analysis were of poor quality. Other forms of bias contributed to heterogeneity in every study. Ultimately, considering the unsatisfactory quality of the included studies, we critically analyzed our recommendations.

A previous meta-analysis suggested that NIV improved survival in acute care settings, whereas subgroup analyses suggested that NIV had no significant effect in multiple subpopulations.^[36] Further, NIV was effective in the treatment

of patients with postoperative acute respiratory failure. However, its role as a preventive tool remains unclear and is probably limited to high-risk patients.^[37] Finally, Olper et al^[38] suggested that NIV was associated with lower reintubation rate after cardiothoracic surgery. However, the type of disease status was not specific and reported outcomes were not comprehensive in previous meta-analyses. In the present study, the overall analysis reported inconsistent conclusions, and subgroup analysis yielded conclusions similar to previous meta-analysis, probably due to the need for updated trial data in additional trials. Our analysis

Table 2**Subgroup analyses based on disease status.**

Outcomes	Group	RR or SMD and 95% CI	P	Heterogeneity, %	P value for heterogeneity
Mortality	Cardiac Surgery	1.38 (0.38 to 5.09)	0.624	41.2	0.147
	Pulmonary Surgery	0.46 (0.22 to 0.95)	0.036	0.0	0.507
Patients showing endotracheal	Cardiac Surgery	0.38 (0.17 to 0.85)	0.019	0.0	0.556
	Pulmonary Surgery	0.71 (0.18 to 2.71)	0.611	69.2	0.039
Respiratory	Cardiac Surgery	0.41 (0.23 to 0.71)	0.001	0.0	0.981
	Pulmonary Surgery	1.08 (0.81 to 1.44)	0.601	0.0	0.595
Cardiovascular	Cardiac Surgery	0.80 (0.59 to 1.09)	0.163	0.0	0.867
	Pulmonary Surgery	2.08 (0.55 to 7.88)	0.283	–	–
Renal	Cardiac Surgery	0.70 (0.26 to 1.92)	0.491	0.0	0.538
	Pulmonary Surgery	–	–	–	–
Other complications	Cardiac Surgery	0.50 (0.16 to 1.58)	0.237	–	–
	Pulmonary Surgery	0.86 (0.40 to 1.79)	0.657	22.8	0.255
Respiratory rate	Cardiac Surgery	0.45 (0.04 to 0.86)	0.033	–	–
	Pulmonary Surgery	–0.68 (–1.27 to –0.10)	0.021	–	–
Heart rate	Cardiac Surgery	0.11 (–0.30 to 0.52)	0.592	–	–
	Pulmonary Surgery	–0.51 (–0.93 to –0.10)	0.016	0.0	0.357
PaO ₂ /FIO ₂ ratio	Cardiac Surgery	–0.22 (–0.56 to 0.12)	0.203	63.4	0.065
	Pulmonary Surgery	0.91 (0.39 to 1.43)	0.001	65.8	0.054
PaCO ₂	Cardiac Surgery	1.09 (–0.17 to 2.35)	0.091	97.8	< 0.001
	Pulmonary Surgery	0.19 (–0.59 to 0.98)	0.629	72.3	0.058
Systolic pressure	Cardiac Surgery	–0.02 (–0.35 to 0.30)	0.891	45.4	0.176
	Pulmonary Surgery	0.01 (–0.55 to 0.58)	0.960	–	–
pH	Cardiac Surgery	0.24 (0.00 to 0.48)	0.048	0.0	0.666
	Pulmonary Surgery	–0.71 (–1.29 to –0.12)	0.018	–	–
Length of ICU stay	Cardiac Surgery	–0.27 (–0.63 to 0.09)	0.144	73.9	0.022
	Pulmonary Surgery	–0.03 (–0.39 to 0.33)	0.874	0.0	0.437
Length of hospital stay	Cardiac Surgery	–0.99 (–2.60 to 0.62)	0.229	98.6	<0.001
	Pulmonary Surgery	0.05 (–0.11 to 0.21)	0.529	0.0	0.411

CI=confidence interval, ICU=intensive care unit, RR=relative risk, SMD=standard mean difference.

suggested that NIV played an important role in specific subpopulations of patients, with no significant effect on the corresponding disease status.

Artificial airway and invasive mechanical ventilation were widely used for patients after cardiothoracic surgery in the treatment of acute respiratory failure. However, artificial airway was always associated with longer ICU and hospital stays, including a higher incidence of ventilator-associated pneumonia and hospital expenditure.^[39] Therefore, effective treatment strategies were needed. NIV was validated as an intervention in the treatment of acute exacerbations of COPD, cardiogenic pulmonary edema, and hypoxemic respiratory failure.^[40] NIV was a promising therapy for patients after cardiac or thoracic surgery, while endotracheal intubation and tracheostomy invasive ventilation were associated with increased severity of complications.^[41] However, inconsistent clinical results were reported, and the efficacy and safety of NIV versus conventional management was not confirmed in patients after cardiac or thoracic surgery. Therefore, we conducted a comprehensive systematic review and meta-analysis to determine the efficacy and safety of NIV versus conventional management. Our study was based on RCTs and explored the possible correlation between NIV use and the outcomes of interest.

In this meta-analysis, the summary RR suggested that NIV reduced the risk of endotracheal intubation by 48%, but was not statistically significant. However, sensitivity analysis indicated potential benefits in reducing the need for endotracheal intubation. Subgroup analysis suggested that NIV was associated with a lower risk of mortality in patients undergoing pulmonary surgery. Further, NIV significantly reduced the risk of endotracheal

intubation in patients undergoing cardiac surgery. Two included trials reported similar results. Our previous study indicated that NIV was indicated for selected patients with acute respiratory failure after cardiac surgery to reduce the need for reintubation. It improved clinical outcomes as compared to conventional treatment. However, pneumonia and a high APACHE II score >20 were independent risk factors of NIV failure in this group of patients.^[34] Finally, Auriant et al^[23] showed that NIV might be safe and effective in reducing the need for endotracheal mechanical ventilation and improved survival after lung resection. Although most trials^[25,26,28] reported no significant endotracheal mechanical ventilation and mortality, they were designed with efficacy of NIV as a primary endpoint, and their sample sizes did not allow adequate power to detect potential clinical differences in endotracheal mechanical ventilation.

Previous results with different disease status were similar to our study.^[21–34] In our study, patients with cardiac surgery, lung resection, and pulmonary lobectomy were included. Insignificant heterogeneity was detected in the risk of mortality or endotracheal mechanical ventilation among the included trials. However, substantial heterogeneity was detected for effective outcomes. Further, few trials reported specific data, such as durations of NIV. Finally, although subgroup analyses suggested that NIV played an important role in multiple outcomes of patients with specific disease status, these conclusions may be unreliable due to the smaller number of trials included in our analysis. Therefore, we were unable to evaluate the effect of NIV duration on treatment outcomes. We merely provided results in patients undergoing NIV as compared to conventional management, and presented a systematic and comprehensive review.

The limitations of the present meta-analysis relate to the small number of included RCTs, most of which were of poor quality. Only 2 trials reported renal complications. Further, we used the definition of efficacy and safety of NIV according to the original trials, and subtle differences between the definitions may have introduced bias. In the present meta-analysis, we observed a high heterogeneity among trials on treatment outcomes index. The included trials were different in terms of results and design, which affected the data and consequently introduced potential bias. Since the number of included trials was small, the findings of subgroup analyses might be unreliable and variable. Fagevik Olsén et al^[26] reported patients who received thoraco-abdominal resection, which included esophagectomy that might bias the conclusion. Finally, the analysis of NIV-associated complications was difficult due to limited data on adverse events reported by a majority of the included studies.

Despite the limitations, our findings have important clinical implications. Previous trials reported inconsistent results on the efficacy and safety of NIV. Systematic reviews and meta-analyses are the most powerful tools in evaluating inconsistencies in efficacy and safety. The findings of this meta-analysis provide evidence supporting the protective role of NIV in specific patient subpopulations. These efficacy and safety findings need further investigation by stratification of potential confounding factors. The summary results for renal complication, other complications, respiratory rate, heart rate, and systolic pressure should be further studied since few trials reported these treatment effects and adverse events.

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