

Meta-analysis of the effects of helmet-assisted non-invasive ventilation in the treatment of acute respiratory failure

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Abstract. – OBJECTIVE: To study the efficacy of helmet-assisted non-invasive ventilation and conventional ventilation in the treatment of acute respiratory failure (ARF).

MATERIALS AND METHODS: Cochrane Library, PubMed, Embase and CNKI databases were searched for randomized controlled trials and case-control trials of helmet-assisted noninvasive ventilation in the treatment of ARF. The outcome measures included respiratory rate, intubation rate, complication rate, mortality rate and arterial blood gas analysis of the commonly used indicators (PaCO₂/PaO₂/pH). The results of the included studies' odds ratio (OR) and its 95% confidential interval (CI) were analyzed using Stata software.

RESULTS: The results of the analysis showed that the in-hospital mortality, intubation rate and complication rate were all significantly decreased with the p-value less than 0.05, which was statistically significant.

CONCLUSIONS: Helmet-assisted noninvasive ventilation can significantly reduce hospital mortality, intubation rate and complication rate, improving the survival rate and prognosis of patients with ARF.

Key Words

Noninvasive ventilation, Helmet-assisted, Acute respiratory failure (ARF), Meta-analysis.

Introduction

Noninvasive ventilation has provided a technology of gas exchange that reduces intubation and mortality. It is now widely used in the treatment of acute respiratory failure (ARF) in patients who have chronic obstructive pulmonary disease (COPD), acute cardiogenic pulmonary edema or thoracic trauma^{1,2}. It is, however, easy to cause complications due to complex conditions and high

technical requirements, and the failure rate reaches 20-30%³. Application of auxiliary facial mask to a great extent reduced the discomfort and complications caused by mechanical ventilation. Although the obvious advantages of auxiliary facial mask, in cases of patients with serious or complicated condition, long-term auxiliary facial mask may inevitably cause complications, such as skin injury, rhinalgia and anabrosis over the bridge of the nose^{4,5}. Also, differences exist in the effects of traditional or auxiliary facial mask ventilation on the intubation rate, mortality or arterial blood gases. Some researches confirmed auxiliary facial mask improves the oxygenation index of patients^{6,7} while others showed there is no difference between traditional and auxiliary facial mask ventilation^{8,9}. Researches¹⁰⁻¹² even indicated auxiliary facial mask increases the re-inhalation of CO₂. In this work, therefore, a meta-analysis was used to detect the efficacy of non-invasive ventilation on ARF patients with emphases on the changes of mortality, intubation rate, respiratory rate, and arterial blood gases.

Materials and Methods

Searching Strategy

Two authors were arranged to search database including Cochrane Library, PubMed, Embase, and CNKI for related literature published from the creation of these databases to December 2018. Keywords used for searching were: "helmet" AND "mechanical ventilation" OR "noninvasive ventilation" OR "facial mask". Experiment objects were limited to patients with ARF caused by various factors. The used language was not limited. References in the included literature were reviewed to remove the repeatedly published literature (Figure 1).

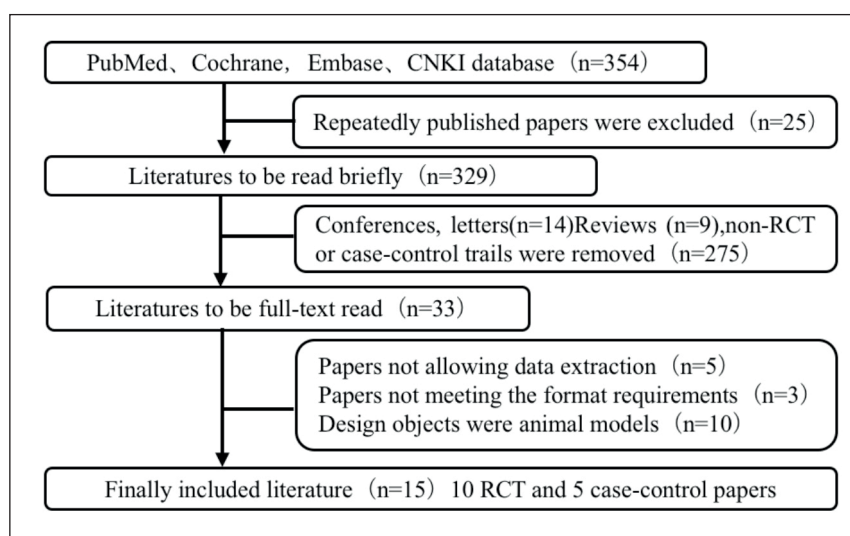


Figure 1. Flow diagram of literature search.

Inclusion and Exclusion Criteria

Two authors were arranged to screen out simultaneously the relevant studies that used conventional ventilation or facial mask auxiliary treatment. Specific inclusion criteria were as follows: (1) The main purpose of the paper was to compare the outcomes of the two methods, including randomized controlled trials (RCT) and case-control trials; (2) the subjects were all adults with ARF; (3) outcome indicators include at least one of the followings: complications, intubation rate, mortality or arterial blood gases. The exclusion criteria: (1) trials of postoperative facial mask application; (2) conference, letters, case report or review of literature; (3) trials without a control group.

Data Extraction and Quality Assessment

Data extraction involved the extraction of general information and outcome indicators in papers. Binary data contained numbers of occurrence and samples in each group. Extraction of continuous data covered the mean, SD and sample size. Tools from Cochrane collaboration network were selected for quality assessment of methodologies containing RCT¹¹. Risks from research design had been assessed according to the following seven entries: random sequence generation, allocation concealment, blinding of participants and appraisers, blinding of outcome evaluation, integrity of result data, selective reporting and other factors. Under each of these entries, it was given “high-risk”, “low-risk” or “unclear” to the information provided. In terms of case-control trials, the Newcastle-Ottawa Scale (NOS) was adopted with the key evaluation points on selectivity, comparability, and exposure factors. A maximum of 9 points would be awarded for each literature. These

above assessments were done independently by two authors that, when in disagreement, had to discuss first and then be arbitrated by a third party.

Statistical Analysis

Meta-analysis was developed for each of the included papers. Binary data were subjected to the combination of odds ratio (OR) and 95% confidence interval (CI) using Mantel-Haenszel method. Effect size from continuous data should be integrated using inverse variance and expressed as standard mean deviation (SMD) with 95% CI. In addition, for studies showing superior inter-study homogeneity, the fixed effect model was used, otherwise the random effect model was applied. Results of heterogeneity detection were determined with the values of I^2 : 25-50% represents a low heterogeneity; 50-75% means moderate; and 75% shows a high heterogeneity¹³.

Results

Literature Search Results

Processes of literature screening have been reported in Figure 1. Preliminary literature was retrieved to 354 related articles, and 25 duplicated articles were excluded. According to the title and abstract of the literature, 298 articles were deleted according to inclusion and exclusion criteria, including 275 non-RCT or case-control trials, 23 reviews and 23 correspondence articles. A total of 33 articles needed to be obtained. 18 articles were excluded through full-text reading. Finally, 15 articles^{6-8,14-25} were included in the meta-analysis, and the basic information of the literature was included (Table I).

Table I. Characteristics of included studies.

Authors	Year	Country	Experiment design	Patients	Treatment group	Control group	Observed outcomes
S Patel et al ¹⁴	2016	America	RCT	ARF caused by ARDS	44	39	Respiratory rate, intubation rate, period of NIV, complications, days without ventilator, hospitalization and mortality, pressure support level, ICU admission
Özlem et al ¹⁶	2015	Turkey	RCT	Hypercapnia ARF	25	23	Respiratory rate, complications, period of NIV, mortality, ICU admission
Pisani et al ¹⁵	2015	Italy	RCT	Hypercapnia ARF	39	41	Respiratory rate, complications, intubation rate, pressure support level, hemodynamic changes
Brambilla et al ¹⁶	2014	Italy	RCT	Hypoxemia ARF	40	41	Intubation rate, hospitalization and mortality, complications
Ali et al ¹⁷	2011	Turkey	RCT	Hypercapnia ARF	15	15	Respiratory rate, intubation rate, complications, ICU admission, hemodynamic changes
Antonaglia et al ¹⁸	2011	Brazil	RCT	Hypercapnia ARF	20	20	Respiratory rate, ICU admission, ventilator assistance
Principi et al ⁷	2004	Italy	Case-control	Hypoxemia ARF	17	17	Intubation rate, complications, period of NIV
Antonelli et al ⁸	2004	Italy	Case-control	Hypercapnia ARF	33	33	Respiratory rate, Intubation rate, complications, days without ventilator, hospitalization and mortality, pressure support level, ICU admission
Rocco et al ¹⁹	2004	Italy	Case-control	Hypoxemia ARF	19	19	Respiratory rate, intubation rate, period of NIV, complications, days without ventilator, hospitalization and mortality, ICU admission
Tonnelier et al ²⁰	2003	France	Case-control	Hypoxemia ARF	11	11	Respiratory rate, complications, in-hospital mortality
Antonelli et al ²¹	2002	Italy	Case-control	Hypoxemia ARF	33	66	Respiratory rate, intubation rate, period of NIV, complications, hospitalization and mortality, pressure support level, ICU admission
Yang et al ²²	2013	China	RCT	COPD/asthma/left heart failure combined with ARF	43	43	Intubation rate, complications, hospitalization and mortality, ICU admission
Wu et al ²³	2011	China	RCT	Hypoxemia ARF	25	25	Complications, arterial blood gas analysis, ICU admission
Xing et al ²⁴	2011	China	RCT	Hypercapnia ARF	20	20	Complications, arterial blood gas analysis, ventilator assistance
Xuan et al ²⁵	2010	China	RCT	Hypoxemia ARF	21	21	Respiratory rate, arterial blood gas analysis, complications

Results of Quality Assessment

As shown in Table II on the quality assessment to case-control studies, the obtained score greater than 4 points was supposed to be a high-quality paper. All the literature clearly reported the outcome indicators in the case and control groups. Figure 2 and 3 showed the results of RCT test evaluation, of which most indicated a low risk, but the “double blinding of participants and personnel” notably suggested a high risk that was inevitable in actual clinical treatment.

Heterogeneity and Publication Bias Test

Both of the two groups were subjected to the combined analysis of complications, mortality, intubation rates, respiratory rates, oxygen pressure, PaCO₂, PaO₂ and pH in the blood. Besides, heterogeneity, publication bias (Begg and Egger) and significance tests were carried out (Table III). The publication bias tests showed there was no bias existing among these included studies.

Meta-Analysis Results

In binary data, 8 studies involving 535 patients reported in-hospital mortalities. The Forest of combined analysis have been shown in Figure 4A where OR=0.50 (95% CI: 0.33-0.78), $p=0.002$. The in-hospital mortality of mask group was 15.4% (39/254) while the in-hospital mortality of non-mask group was 29.2% (82/281). 11 studies containing 685 patients reported intubation rates as shown in Figure 4B where OR=0.39 (95% CI: 0.27-0.56), $p=0.000$. The intubation rate in mask group was 14.9% (49/328) while the intubation rate in non-mask group 38.4% (137/357). 10 studies including 637 patients gave the occurrence rate of complications. Their Forest of combined analysis were shown in Figure 4C where OR=0.57 (95% CI: 0.39-0.84) and $p=0.04$. Occurrence rate of complications in mask group was 16.8% (51/304) and the occurrence rate of complications in non-mask group 31.5% (105/333). As for continuous data, two groups of contrastive analysis in terms of respiratory rate, PaCO₂, PaO₂ and pH, were reported (Figure 5). Considering the high heterogeneity, random effect model was selected for combined analysis which then showed in the results that both the respiratory rate and PaCO₂ of the facial mask auxiliary ARF group were lower than that of the control group: SMD=-0.28 (95% CI: -0.77~0.21), $p=0.262$; SMD=-0.29 (95% CI: -1.04~0.47), $p=0.457$; the PaO₂ and pH were inversely higher than that of the control group: SMD=0.28 (95% CI: -0.11~0.67), $p=0.153$; SMD=0.24 (95% CI: -0.32~0.79), $p=0.399$.

There was no difference between subgroups and the combined analyses. Subgroup analysis showed that in those included RCT trails, patients who underwent auxiliary laryngeal mask ventilation have significantly reduced the occurrence rate of complications and mortality ($p<0.001$) (Figure 4A-B), but higher intubation rates than those in case-control trails. From subgroup analyses of respiratory rate, PaCO₂, PaO₂ and pH, the results of RCT and case-control trails were basically consistent (Figure 5), that is, auxiliary laryngeal mask may not have greatly improved the respiratory rate, PaCO₂, PaO₂ or pH of patients with ARF.

Discussion

As shown in the comparison between auxiliary laryngeal mask and conventional ventilation, mask auxiliary noninvasive ventilation greatly reduced the mortality, intubation rate, and occurrence of complications, but showed little effects on the PaCO₂, PaO₂ or pH. Noninvasive respirator supports respiration without endotracheal stoma or tracheostoma. Wearing auxiliary facial mask, patients have full access to the respirator by the nose, mouth and face, avoiding damage in airway or of swallowing ability. Appropriate respiratory support with auxiliary facial mask may reduce the mortality of ARF patients^{26,27}. However, it should be noted that persistent mask wearing probably makes the patient uncomfortable, lowers the therapeutic effects or even increases the occurrence of complications²⁸⁻³⁰. This meta-analysis involving RCT and case-control trails indicated that noninvasive ventilation with auxiliary facial mask lowered in-hospital mortality, i.e. the mask itself may enhance the survival rate of patients with ARF. This is a specific advantage that any other ventilatory support cannot provide. In the first place, ventilation with auxiliary facial mask impacts little on patients' diet or verbal communication; secondly, patients are highly tolerant to facial mask auxiliary ventilation, elevating the success rate of noninvasive treatment. Furthermore, respiratory support with auxiliary facial mask accommodates to more critical illnesses and even variation coming from different appearances. In short, auxiliary facial mask improved the comfort through the ventilatory support and was well tolerated by patients, let alone the reduced occurrence of pneumonia, in-hospital mortality and other factors. It was suggested to generally accept the application of auxiliary mask.

Table II. NOS score of case-control studies.

Authors	Year	Selection				Comparability		Exposure			Overall stars
		Is the case definition adequate?	Representative of the cases	Selection of controls	Definition of controls	Control for important factors	Control for additional factors	Ascertainment of exposure	Same method of ascertainment cases and controls	Non response rate	
Principi et al ⁷	2004	*	*	*	*	*	*	*	*	-	8
Antonelli et al ⁸	2004	*	*	-	*	*	-	*	-	-	5
Rocco et al ¹⁹	2004	*	*	-	*	*	-	*	-	-	5
Tonnelier et al ²⁰	2003	*	*	-	*	*	*	*	-	-	6
Antonelli et al ²¹	2002	*	*	-	*	*	*	*	-	-	6

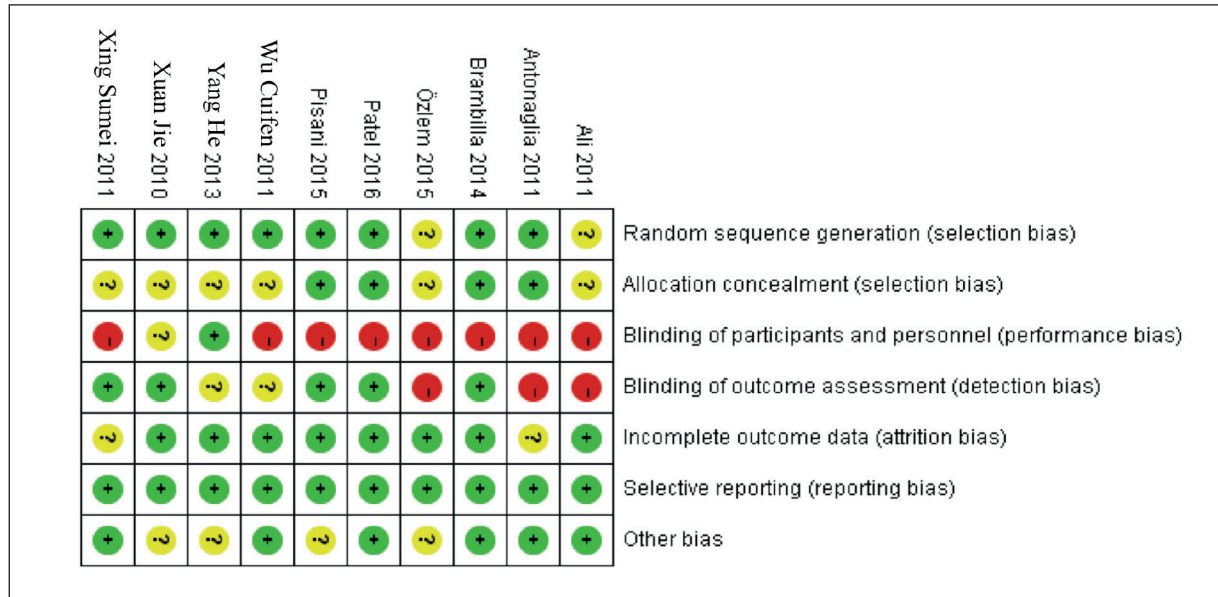


Figure 2. Summary of each risk item of RCT.

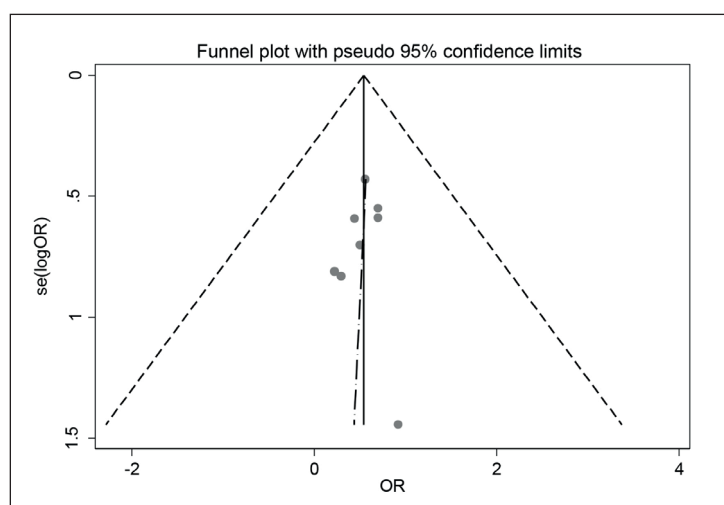


Figure 3. Funnel plots of public bias.

What worthy of attention is ventilatory support with auxiliary facial mask reduces the in-hospital complications and mortality. Several studies have attempted to demonstrate the efficacy of mask auxiliary noninvasive ventilation in patients with ARF, but the prognosis is limited probably due to different breathing patterns of ARF patients caused by acid-base imbalance: mouth breathing is more common in patients with hypoxemia, leading to a better effect of mask auxiliary. This, however, does not mean that auxiliary mask noninvasive ventilation will not impact the mortality of ARF patients. Two small-sample studies have found that, for ARF patients with hypercapnia, ventilatory support with auxiliary facial mask improves survival rate, but it was still not hard evidence. Further researches are needed.

Conclusions

This meta-analysis indicated auxiliary mask noninvasive ventilation made the prognosis of ARF patients better and reduced the rate of intubation and complications. Auxiliary mask could enhance the gas exchange efficiency. Nevertheless, it was worth noting that the advantages of facial mask application have not been scientifically evidenced so more RCT or case-control trails are strongly needed to support the reliability.

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Conflict of Interests

The authors declare that they have no conflict of interests.

Table III. Heterogeneity and publication bias test.

Index	Analysis model	Heterogeneity		Begg		Egger		X ²	
		I ² (%)	p	z	p	t	p	z	p
Complications	Fixed	47.7	0.045	0.09	0.929	0.02	0.988	2.89	0.04*
Mortality	Fixed	0%	0.935	-1.24	0.216	-0.37	0.725	3.11	0.002**
Intubation rate	Fixed	19.3	0.259	0.08	0.938	0.08	0.938	5	0***
Respiratory rate	Random	80.2	0	0.45	0.652	-0.22	0.835	1.12	0.262
PaCO ₂	Random	92.1	0	-1.04	0.297	-0.62	0.558	0.74	0.457
PaO ₂	Random	75.1	0	-0.27	0.788	0.14	0.894	1.43	0.153
pH	Random	86.3	0	1.88	0.061	2.38	0.049	0.84	0.399

Notes: *0.05, **0.01, ***0.001.

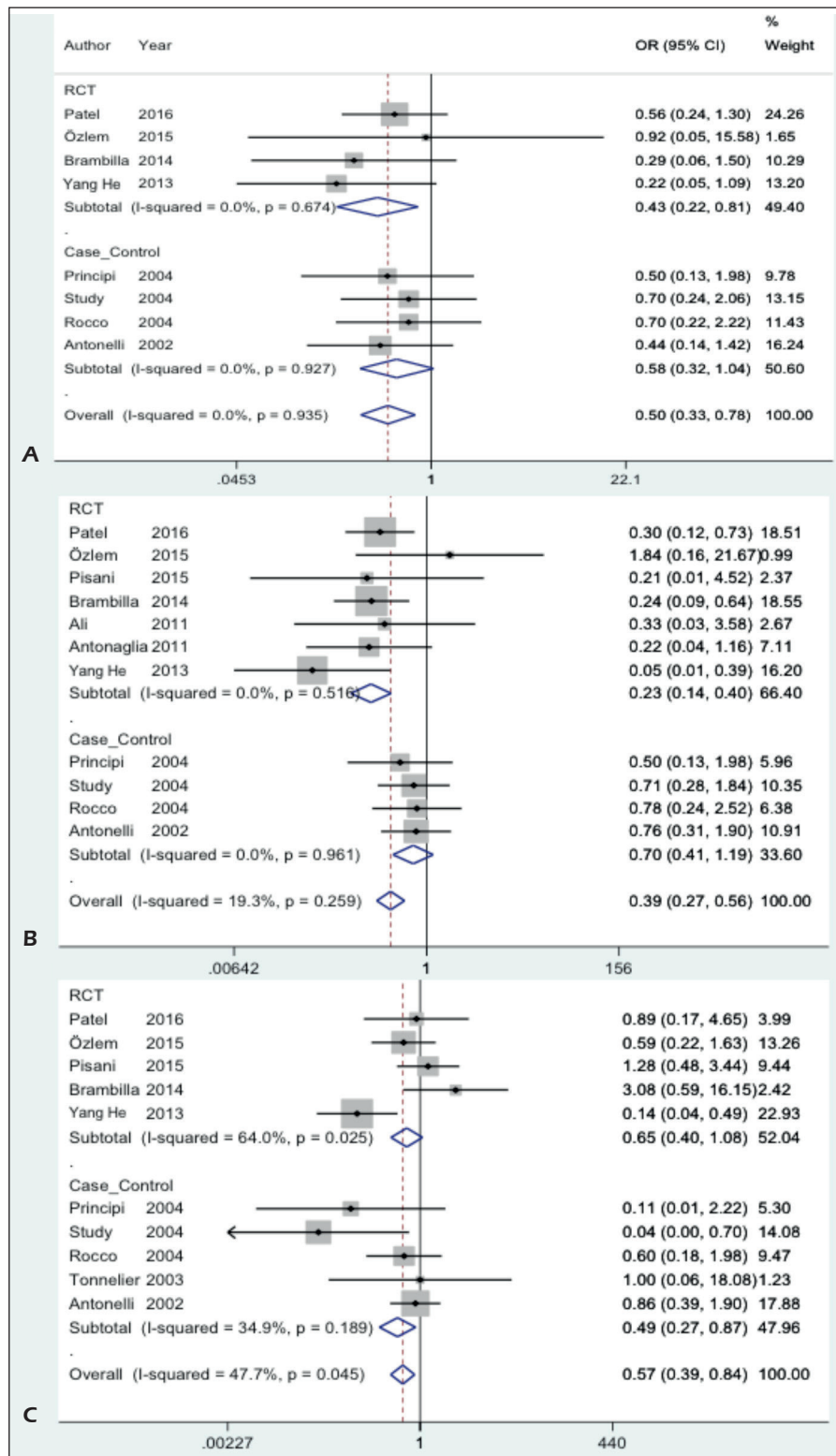


Figure 4. Forests of binary data. **A.** Forest gram of in-hospital mortality ratio. **B.** Forest gram of complications ratio. **C.** Forest gram of intubation ratio.

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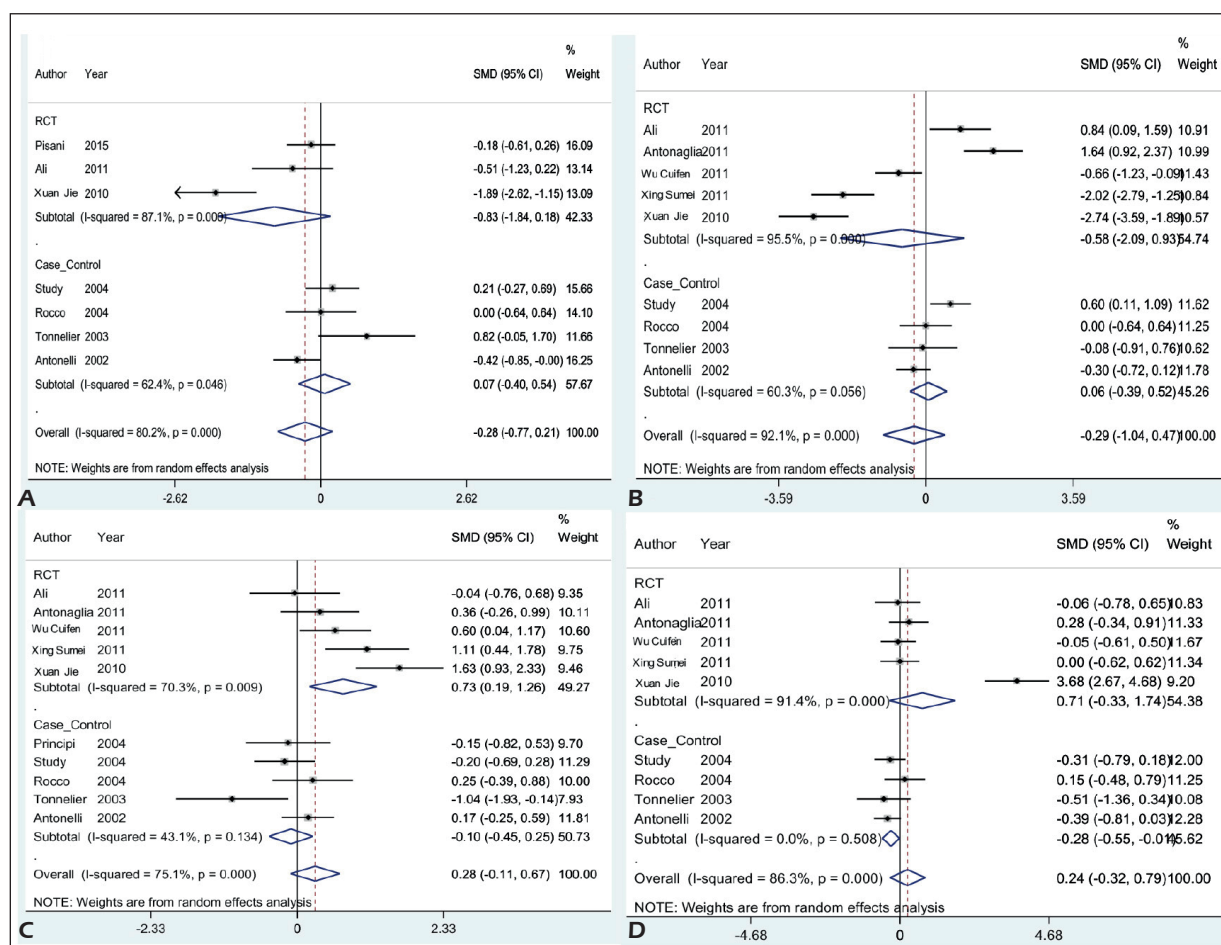


Figure 5. Forests of continuous data. **A**, Forest gram of respiratory rate ratio. **B**, Forest gram of PaCO₂ ratio. **C**, Forest gram of PaO₂ ratio. **D**, Forest gram of pH ratio.

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