



## Noninvasive ventilation for acute lung injury a meta-analysis of randomized controlled trials



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### ABSTRACT

**Purpose:** To compare the effect of noninvasive ventilation (NIV) and standard oxygen therapy on treating acute lung injury (ALI).

**Methods:** A search on PubMed, Embase, Springer, Cochrane Central Register of Controlled Trials and Clinical Trials was carried out up to Nov 2015 for randomized controlled trials (RCTs) with NIV as cases and standard oxygen therapy as controls. Risk ratios and weight mean difference were used for estimation.

**Results:** This meta-analysis included seventeen RCTs. Results showed NIV significantly reduced the intubation rate, length of ICU stay and hospital mortality. The length of hospital stay and ICU mortality were not different. High heterogeneity was found across the studies of intubation rate. The types of acute respiratory failure might be a source of heterogeneity.

**Conclusion:** Our results suggest that NIV is effective for ALI in reducing the intubation rate, hospital mortality and length of ICU stay than the standard oxygen therapy.

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### Introduction

Acute lung injury (ALI) is a syndrome consisting of acute hypoxemic respiratory failure with bilateral pulmonary infiltrates. It is associated with both pulmonary and non-pulmonary risk factors.<sup>1,2</sup> Moreover, there is a great possibility that these pulmonary and non-pulmonary risk factors would develop into acute respiratory failure or acute respiratory distress syndrome (ARDS). Advances in the pathophysiology, treatment and long-term outcome of ALI have been developed.<sup>3–5</sup> Both intubation and mechanical ventilation were usually required for severe acute respiratory failure patients.<sup>6</sup> Studies have indicated that the use of artificial airway and invasive ventilation may result in more sedative use and airway trauma,

which increases the risk of ventilator associated pneumonia (VAP), as well as the hospital length of stay, morbidity and mortality.<sup>7,8</sup> As progress moves far ahead, the noninvasive ventilation (NIV) using assisted mechanical ventilation without the need for an invasive artificial airway is developed and successfully applied in ALI and respiratory failure patients.<sup>9,10</sup>

Recently, NIV, such as noninvasive positive pressure ventilation (NIPPV) and continuous positive airway pressure (CPAP), has been increasingly widespread in the treatment of ALI, respiratory failure and ARDS, but its effect remains controversial. In Antonelli's report, early administration of NIV was well tolerated and associated with a significant reduction in the rate of endotracheal intubation, fatal complications, and intensive care unit (ICU) mortality in a group of organ transplant recipients with respiratory failure.<sup>9</sup> However, in a similar eighty-one patients study, it demonstrated that there was no difference in the need for re-intubation, the length of stay, or mortality between the patients with application of NIV and standard management.<sup>11</sup> Recently, a meta-analysis of 87 RCTs focusing on the outcome of mortality has been published<sup>12</sup> however without estimation of other outcomes like intubation rate and length of hospital and ICU stay.

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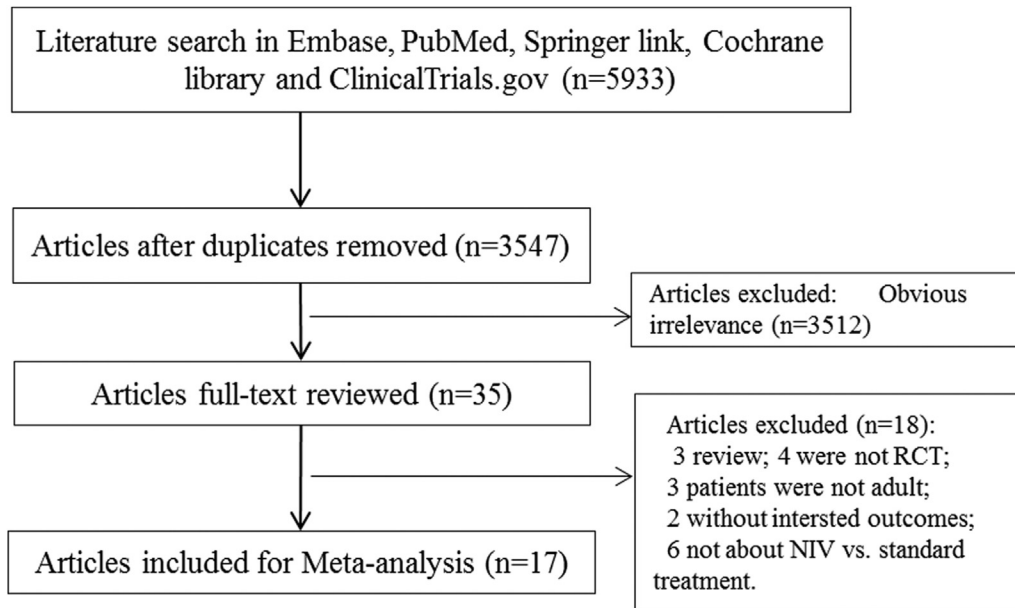


Fig. 1. Literature search and study selection.

To comprehensively evaluate the security of NIV treatment for ALI, respiratory failure and/or ARDS patients, we performed a systematic review and meta-analysis by evaluating the intubation rate, length and mortality of ICU stay and hospital stay of NIV on treating ALI and respiratory failure.

## Methods

### Source of material

Articles from databases, including PubMed, Springer, Cochrane Central Register of Controlled Trials and Clinical Trials (ClinicalTrials.gov) were retrieved with a deadline of Nov. 17, 2015. The keywords used for all searches were as follows: 1) research interventions including “noninvasive ventilation (NIV),” “noninvasive positive pressure ventilation (NIPPV),” “continuous positive airway pressure (CPAP),” “bilevel positive airway pressure (BiPAP)” AND 2) research objects of “acute lung injury (ALI)” and “acute respiratory distress syndrome (ARDS)” or “acute respiratory failure.” Meanwhile, references from retrieved papers were checked for additional studies. Data from full-published English paper were collected, and references of reviews were also reviewed artificially.

### Study selection criteria

Studies meeting the following criteria were included in the meta-analysis: 1) the study was designed as a randomized controlled trial (RCT); 2) the subjects were adults ( $\geq 18$  years old) who were clinically diagnosed with ALI or acute respiratory failure; 3) the interventions in case group included NIV, NIPPV, CPAP and BiPAP; 4) the control treatment was standard oxygen therapy or conventional oxygen therapy; 5) the outcomes such as intubation rate, death rate (mortality), length of ICU stay and length of hospital stay were evaluated.

Studies were excluded under the following conditions: 1) research subjects were newborns, children or minors; 2) articles were non-original literature such as reviews, letters or comments; 3) studies with continuous variable data that were not expressed as mean  $\pm$  standard deviation were also excluded.

### Data extraction and quality evaluation

Two reviewers independently evaluated the quality of relevant articles and identified eligible studies from the databases. Data items included the first author's name, year of publication, research time and area, age and gender distribution of participants, the ventilator mode, parameters and connection of the breathing machine, and outcomes were extracted. Disagreement would be settled by discussing with another reviewer. Evaluation of research quality was managed with Review Manager Version 5.0 (RevMan 5.0) software using Cochrane risk of bias tool.

### Data analysis

Data analyses were performed using RevMan 5.0 provided by the Cochrane Collaboration. The results of the meta-analysis were shown by graphical displays of forest plots. Risk ratio (RR) or weight mean difference (WMD) with their 95% confidence intervals (CIs) were calculated as effect sizes. RR was calculated for dichotomous data, while WMD was applied for continuous variables. Heterogeneity between studies was assessed by testing Cochran's Q-statistic<sup>13</sup> and  $I^2$ .<sup>14</sup> A significant Q-statistic ( $P < 0.10$ ) or  $I^2$ -statistic ( $I^2 > 50\%$ ) indicated significant heterogeneity across studies, then the random-effects model (DerSimonian and Laird method) would be used for meta-analysis. Otherwise, the fixed-effect model (Mantel-Haenszel method) would be applied. Subgroup analysis based on the type of acute respiratory failure (acute respiratory failure, post-operative acute respiratory failure, postextubation acute respiratory failure) was performed. All the  $P$  values were two-sided. The  $P < 0.05$  was considered to be statistically significant, except for heterogeneity analysis.

## Results

### Study selection

Details of the study selection are presented in a flow diagram (Fig. 1). There were 5933 papers originally applicable to the

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