

# High-Flow Nasal Cannula vs Conventional Oxygen Therapy for Postcardiothoracic Surgery

Yiwei Wang, Dong Huang, Yuenan Ni, and Zongan Liang

**BACKGROUND:** High-flow nasal cannula (HFNC) oxygen therapy is widely used in extubated patients. We aim to evaluate the effect of HFNC compared with conventional oxygen therapy in adults after cardiothoracic surgery. **METHODS:** We conducted a literature search in PubMed, Embase, and ClinicalTrials for randomized controlled trials that compared HFNC with conventional oxygen therapy in extubated patients after cardiothoracic surgery. **RESULTS:** Eight studies with 1,086 subjects were included. Compared with conventional oxygen therapy, HFNC was associated with a significant reduction in the need for escalation of respiratory support (risk ratio 0.40, 95% CI 0.26–0.61,  $P < .001$ ), re-intubation rate (risk ratio 0.35, 95% CI 0.13–0.96,  $P = .04$ ), and length of hospital stay (mean difference  $-0.48$ , 95% CI  $-0.95$  to  $-0.01$ ,  $P = .05$ ). No significant differences were found for the length of ICU stay (mean difference  $-0.09$ , 95% CI  $-0.21$  to  $-0.04$ ,  $P = .18$ ), pulmonary complications (risk ratio 0.85, 95% CI 0.48–1.48,  $P = .56$ ), or mortality rate (risk ratio 0.54, 95% CI 0.12–2.53,  $P = .44$ ). **CONCLUSIONS:** HFNC may significantly reduce the need for the escalation of respiratory support and re-intubation rate, and might reduce the hospital stay. More high-quality randomized controlled trials are needed to further validate our results. *Key words:* cardiothoracic surgery; high-flow nasal cannula; oxygen therapy; respiratory support. [Respir Care 2020;65(11):1730–1737. © 2020 Daedalus Enterprises]

## Introduction

More than 1.5 million cardiothoracic surgeries worldwide require mechanical ventilation and extubation every year.<sup>1</sup> Oxygen therapy after extubation is often needed to maintain oxygenation in the postoperative period. Conventional oxygen therapy delivers a low flow of oxygen through a nasal

cannula or face mask. However, after cardiothoracic surgery, patients usually have atelectasis and pleural effusions, which make them prone to pulmonary complications and respiratory failure.<sup>2</sup> These complications are associated with increased morbidity and mortality, prolonged hospital stay, and higher costs.<sup>3</sup> The maximum flow delivered by conventional oxygen therapy devices is limited. As an alternative to conventional oxygen therapy, high-flow nasal cannula (HFNC) oxygen therapy has been increasingly studied.<sup>4,5</sup>

HFNC is a technique that delivers heated and humidified oxygen through nasal cannulae.<sup>6</sup> At the air/oxygen blender,  $F_{IO_2}$  is set at 0.21–1.0 at a flow of up to 60 L/min. Compared with conventional oxygen therapy, HFNC can provide a high fraction of inspired oxygen to improve oxygenation and produces PEEP dependent on the flow to counteract auto-PEEP, preventing supraglottic collapse, reducing nasopharyngeal resistance, and reducing the work of breathing.<sup>7</sup>

HFNC is increasingly being used after extubation for surgical and nonsurgical patients for the prevention and treatment of respiratory failure.<sup>8,9</sup> After cardiothoracic surgery, patients are usually sent to the ICU to continue receiving invasive mechanical ventilation for a period of time. When patients meet the requirements for extubation, the best

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The authors are affiliated with the Department of Respiratory and Critical Care Medicine, West China School of Medicine and West China Hospital, Sichuan University, Chengdu, Sichuan, China.

Drs Wang and Huang contributed equally to this work.

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Correspondence: Zongan Liang MD, Department of Respiratory and Critical Care Medicine, West China School of Medicine and West China Hospital, Sichuan University, No. 37 Guoxue Alley, Chengdu, 610041, Sichuan, China. E-mail: [liangzongan817@163.com](mailto:liangzongan817@163.com).

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choice of oxygen therapy among the various oxygen therapy devices is a matter of debate.<sup>10</sup> Therefore, we performed a systematic review and meta-analysis to identify the latest evidence for clinical practice.

## Methods

This meta-analysis was conducted in adherence to the Cochrane Handbook for Systematic Reviews and Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) statement.<sup>11</sup> Each included clinical trial was approved by the corresponding institutional ethical committee. Written informed consent was provided by the participants of each study.

## Search Strategy

We searched PubMed, Embase, and ClinicalTrials from inception to November 2019 using search strategies adapted to each database, including Medical Subject Headings (MeSH) and key words (ie, “high-flow nasal cannula oxygen,” “high-flow oxygen therapy,” “high-flow nasal therapy,” “humidified high-flow nasal cannula,” “thoracic surgery,” “thoracic surgical procedures,” “pulmonary surgical procedures,” and “pneumectomy”) without limitations on publication type or language. We also reviewed the references of relevant studies to identify additional suitable articles. Two investigators (YW, DH) independently screened the titles and abstracts using relevant, irrelevant, or unsure designations. Disagreements were resolved by discussion with a third investigator (ZL).

HFNC oxygen therapy was defined as using the heated humidifier device and nasal cannula to deliver oxygen. Conventional oxygen therapy was defined as oxygen delivery using low-flow devices such as nasal cannulae or masks. Eligible studies were identified according to the following inclusion criteria: (1) randomized controlled trials, (2) adult subjects undergoing cardiothoracic surgery, (3) comparisons of HFNC with conventional oxygen therapy after extubation, and (4) inclusion of at least one of the predetermined outcomes. We excluded observational studies and studies published as reviews, letters, case reports or conference abstracts.

## Outcomes

The primary outcome was the escalation of respiratory support, defined as the change to noninvasive ventilation or invasive mechanical ventilation in the HFNC group and the change to noninvasive ventilation, HFNC, or invasive mechanical ventilation in the conventional oxygen therapy group. Secondary outcomes were re-intubation rate, length of ICU stay, length of hospital stay, pulmonary complications including postoperative pneumonia and atelectasis, and mortality rate.

## Quality Assessment

The quality of the included studies was assessed with the Cochrane Risk of Bias Tool for Randomized Controlled Trials and rated as low risk, unclear risk, or high risk.<sup>12</sup> Studies were evaluated according to the following domains: blinding of participants and personnel, random sequence generation, allocation concealment, incomplete outcome data, blinding for outcome assessment, selective outcome reporting, and other sources of bias.

## Statistical Analysis

Studies were tested for heterogeneity using the  $I^2$  statistic, and an  $I^2$  value > 50% indicated substantial heterogeneity.<sup>13</sup> We used fixed-effects models to pool data with insignificant heterogeneity and random-effects models when significant heterogeneity was identified. We also carried out sensitivity analysis by excluding one trial in each turn to test the influence of a single study on the overall pooled estimate.

We undertook this meta-analysis using Review Manager 5.3 (Cochrane Collaboration, Oxford, United Kingdom). The data were obtained by direct extraction or by indirect calculation. Dichotomous outcomes were presented as risk ratios and 95% CIs. Continuous outcomes were presented as mean differences and 95% CIs. For studies reporting medians with accompanying interquartile ranges (IQRs) or ranges, we estimated the mean and SD prior to data analysis.<sup>14,15</sup> The results were displayed graphically using forest plots, and the potential publication bias was analyzed by visual inspection of the funnel plot. All statistical tests were 2-sided, and statistical significance was defined as a  $P < .05$ .

## Results

### Study Selection

A total of 663 articles were identified through the database searching and other sources. After the removal of 47 duplicates, the title and abstract of 616 studies were screened. We identified 31 articles as potentially relevant, and the full articles were read. Finally, 8 articles met our inclusion criteria and were selected for data extraction, analysis, and quality assessment.<sup>16-23</sup> A flow chart of the search strategy and the reasons for exclusion are shown in Figure 1.

### Study Characteristics

Eight randomized controlled trials involving a total of 1,086 cardiothoracic surgical subjects were included in this meta-analysis. In the included studies, 542 subjects re-

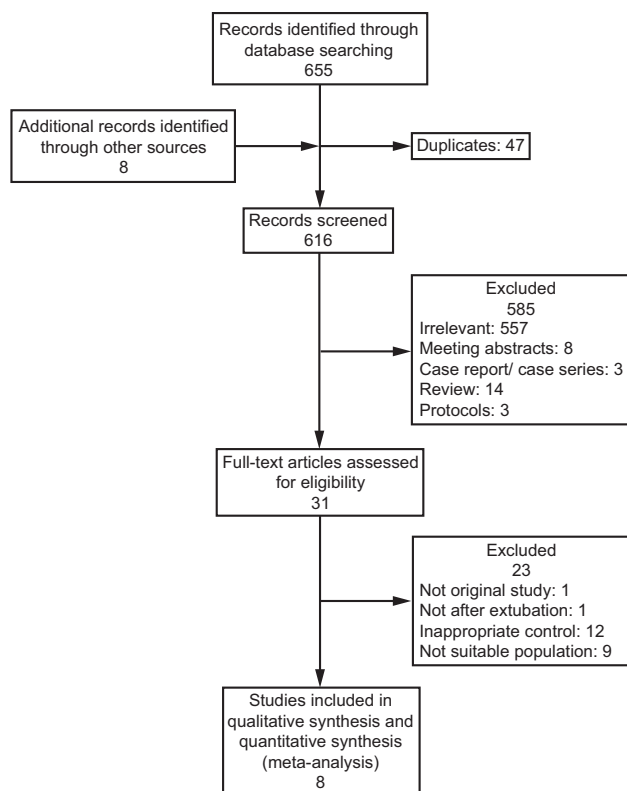


Fig. 1. Flow chart.

ceived HFNC and 544 subjects received conventional oxygen therapy. The basic demographic characteristics of the included studies are shown in Table 1. The risk of bias for each study was evaluated. Due to the significant difference between HFNC and conventional oxygen therapy devices, none of the studies included were double-blind. The details of the risk of bias assessment are shown in Table 2.

### Escalation of Respiratory Support

Six studies including 894 subjects reported the rate of respiratory support escalation. There were significant differences between the HFNC and the conventional oxygen therapy groups (risk ratio 0.40, 95% CI 0.26–0.61,  $P < .001$ ,  $I^2 = 0\%$ ). Subgroup analysis was conducted according to different surgeries, and the results showed that HFNC significantly reduced the escalation of respiratory support for subjects who underwent cardiac surgery (risk ratio 0.46, 95% CI 0.29–0.74,  $P = .001$ ,  $I^2 = 0\%$ ) and for subjects who underwent thoracic surgery (risk ratio 0.23, 95% CI 0.08–0.66,  $P = .006$ ,  $I^2 = 49\%$ ) (Fig. 2).

### Re-intubation Rate

Five studies including 800 subjects reported the re-intubation rate. The HFNC group showed a significantly lower

re-intubation rate than the conventional oxygen therapy group (risk ratio 0.35, 95% CI 0.13–0.96,  $P = .04$ ,  $I^2 = 24\%$ ) (Fig. 3).

### Length of ICU and Hospital Stay

Eight studies including 1,086 subjects reported the ICU stay. No significant differences were found between the HFNC group and the conventional oxygen therapy group (mean difference 0.09, 95% CI –0.21–0.04,  $P = .18$ ,  $I^2 = 9\%$ ) (see the supplementary materials at <http://www.rcjournal.com>). Seven studies including 931 subjects reported the length of hospital stay. Subjects in the HFNC group had a shorter length of hospital stay than those in the conventional oxygen therapy group (mean difference –0.48, 95% CI –0.95 to –0.01,  $P = .05$ ,  $I^2 = 64\%$ ) (Fig. 4).

### Pulmonary Complications

Four studies including 349 subjects reported pulmonary complications for pneumonia and atelectasis. There were no significant differences between the HFNC group and the conventional oxygen therapy group (risk ratio 0.85, 95% CI 0.48–1.48,  $P = .56$ ,  $I^2 = 0\%$ ) (see the supplementary materials at <http://www.rcjournal.com>).

### Mortality Rate

Five studies including 691 subjects reported the mortality rate. Our meta-analysis demonstrated no significant difference in the mortality rate between the HFNC group and the conventional oxygen therapy group (risk ratio 0.54, 95% CI 0.12–2.53,  $P = .44$ ,  $I^2 = 0\%$ ) (Fig. 5).

### Publication Bias

No obvious publication bias was observed in a visual inspection of the funnel plots in our meta-analysis (see the supplementary materials at <http://www.rcjournal.com>).

### Discussion

Our systematic review and meta-analysis suggested that HFNC was associated with less escalation of respiratory support, lower re-intubation rate, and possibly a shorter hospital stay than conventional oxygen therapy after cardiothoracic surgery. No significant differences were found for the length of ICU stay, incidence of pulmonary complications, or mortality rate between the 2 groups.

Our results indicate that HFNC might have the advantages of reducing the need to escalate respiratory support compared with conventional oxygen therapy. These findings were similar to the meta-analysis published by Lu

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Table 1. Characteristics of Included Studies

Study	Year	Type of Surgery	Subject Characteristics (HFNC Group, Conventional Oxygen Therapy Group)				Outcomes
			Subjects, <i>n</i>	Target SpO <sub>2</sub> , %	Age, y	Body Mass Index, kg/m <sup>2</sup>	
Parke et al <sup>16</sup>	2013	Cardiovascular surgery	169, 171	> 93%	65, 66	28.4, 29.2	Escalation of respiratory support Re-intubation rate ICU stay Hospital stay Pulmonary complications Mortality
Corley et al <sup>17</sup>	2015	Cardiovascular surgery	81, 74	≥ 95%	63, 65	36, 35	Escalation of respiratory support Re-intubation rate ICU stay
Yu et al <sup>19</sup>	2017	Thoracoscopic lobectomy	56, 54	≥ 95%	56.3, 55.8	26.3, 25.2	Escalation of respiratory support Re-intubation rate ICU stay Hospital stay Pulmonary complications Mortality
Brainard et al <sup>18</sup>	2017	Thoracic surgery	18, 26	≥ 90%	57, 59	26, 25	ICU stay Hospital stay Pulmonary complications
Zochios et al <sup>21</sup>	2018	Cardiac surgery	49, 45	≥ 95%	67.3, 69.1	32, 30.2	Escalation of respiratory support ICU stay Hospital stay Mortality
Sahin et al <sup>20</sup>	2018	Cardiopulmonary bypass	50, 50	> 93%	62.0, 61.3	32.5, 32.3	Escalation of respiratory support Re-intubation rate ICU stay Hospital stay Pulmonary complications Mortality
Tatsuishi et al <sup>23</sup>	2019	Coronary artery bypass graft surgery	72, 76	≥ 94%	69, 69	NA	ICU stay Hospital stay
Pennisi et al <sup>22</sup>	2019	Lung resection	47, 48	92–98%	66, 68	26, 27	Escalation of respiratory support Re-intubation rate ICU stay Hospital stay Pulmonary complications Mortality

All studies included in this meta-analysis were randomized controlled trials.  
 HFNC = high-flow nasal cannula  
 NA = not available

et al,<sup>24</sup> which included both randomized controlled trials and observational studies for all types of postoperative subjects. Lu et al<sup>24</sup> also mentioned that the type of surgery might affect the determination of the primary outcome. In our study, we performed a subgroup analysis for the primary outcome and found that the HFNC group had lower escalation of respiratory support for subjects after both cardiac and thoracic surgery. Several mechanisms might be

responsible for the efficacy of HFNC, including the most direct effect of high oxygen which washes out CO<sub>2</sub>, thus decreasing dead space and rebreathing, while increasing effective alveolar ventilation.<sup>25-27</sup> In addition, HFNC creates a positive pressure space, which dilates the nasopharyngeal radius of the airway and dramatically reduces nasopharyngeal resistance and the work of breathing. After cardiothoracic surgery, patients are likely to experience

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Table 2. Quality Assessment of Randomized Controlled Trials Included in Analysis

Author, Year	Random Assignment	Allocation Concealment	Blinding of Participants	Blind Evaluation for Outcomes	Incomplete Outcome Data	Selective Reporting	Other Bias
Parke et al <sup>16</sup>	Low risk	Low risk	High risk	Low risk	Low risk	Low risk	Low risk
Corley et al <sup>17</sup>	Low risk	Low risk	High risk	Low risk	Low risk	Low risk	Low risk
Yu et al <sup>19</sup>	Low risk	Low risk	High risk	Unclear risk	Low risk	Low risk	Low risk
Brainard et al <sup>18</sup>	Low risk	Low risk	High risk	Unclear risk	Unclear risk	Low risk	Low risk
Zochios et al <sup>21</sup>	Low risk	Low risk	High risk	Low risk	Low risk	Low risk	Low risk
Sahin et al <sup>20</sup>	Low risk	Unclear risk	High risk	Low risk	Low risk	Low risk	Low risk
Tatsuiishi et al <sup>23</sup>	Low risk	Unclear risk	High risk	Low risk	Low risk	Low risk	Low risk
Pennisi et al <sup>22</sup>	Low risk	Low risk	High risk	Unclear risk	Low risk	Low risk	Low risk

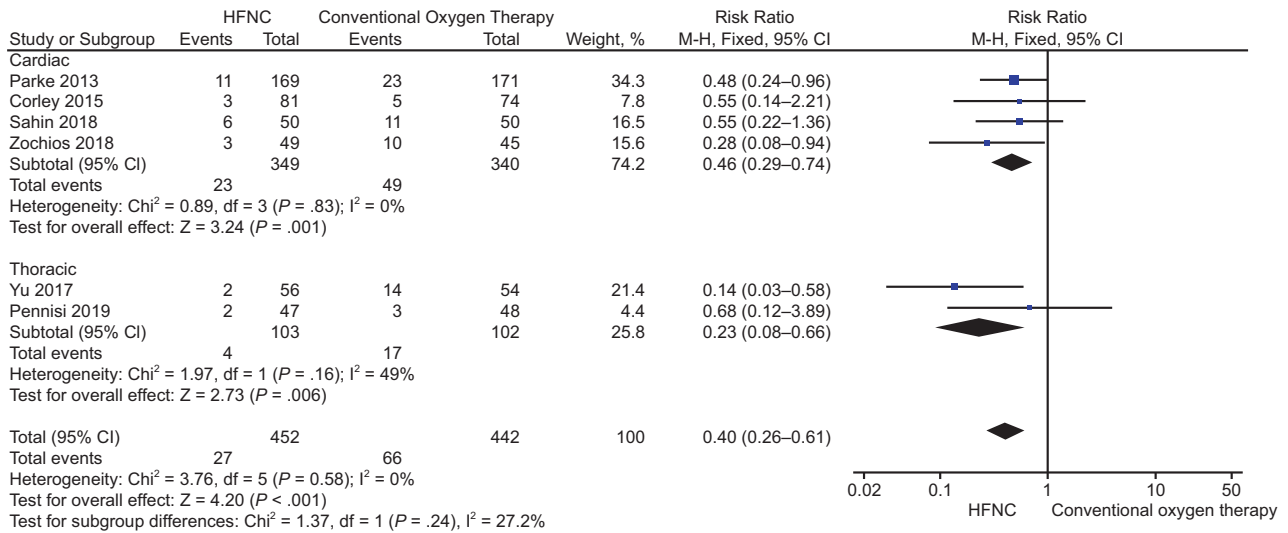


Fig. 2. Escalation of respiratory support. HFNC = high-flow nasal cannula; M-H = Mantel-Haenszel.

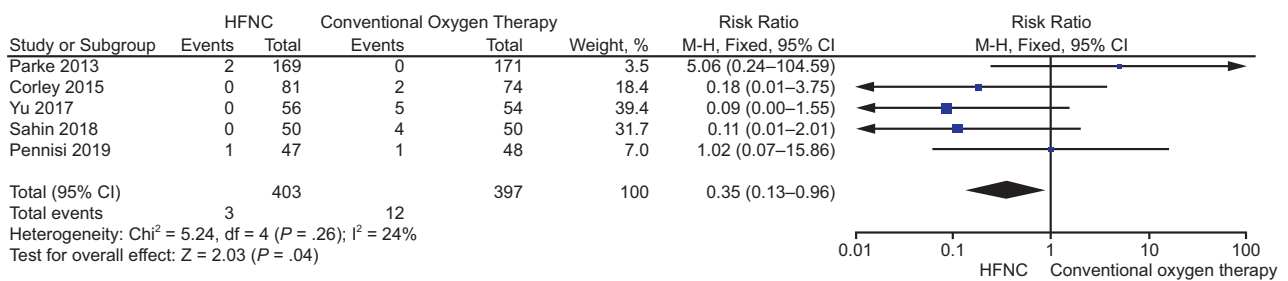


Fig. 3. Re-intubation rate. HFNC = high-flow nasal cannula; M-H = Mantel-Haenszel.

pain, anesthesia-induced atelectasis, decreased movement of respiratory muscles, and diminished functional residual capacity.<sup>28</sup> The maximum flow is low for most conventional oxygen therapies, which leads to a significant decrease in F<sub>IO<sub>2</sub></sub>. HFNC is better than conventional oxygen therapy in providing more effective alveolar oxygen delivery, improving mucociliary clearance, and reducing the work of breathing, thus increasing alveolar recruitment and improving oxygenation for these patients.<sup>29,30</sup>

We also observed a significantly lower re-intubation rate in the HFNC group. HFNC has resulted in better physiological outcomes, such as lower heart rate and higher P<sub>aO<sub>2</sub></sub> than conventional oxygen therapy.<sup>31</sup> These physiological indicators might directly affect a clinician's assessment of whether a postcardiothoracic surgery patient requires re-intubation. For patients who need invasive mechanical ventilation, delayed intubation can lead to increased mortality.<sup>32</sup> The failure of initial noninvasive oxygen therapies



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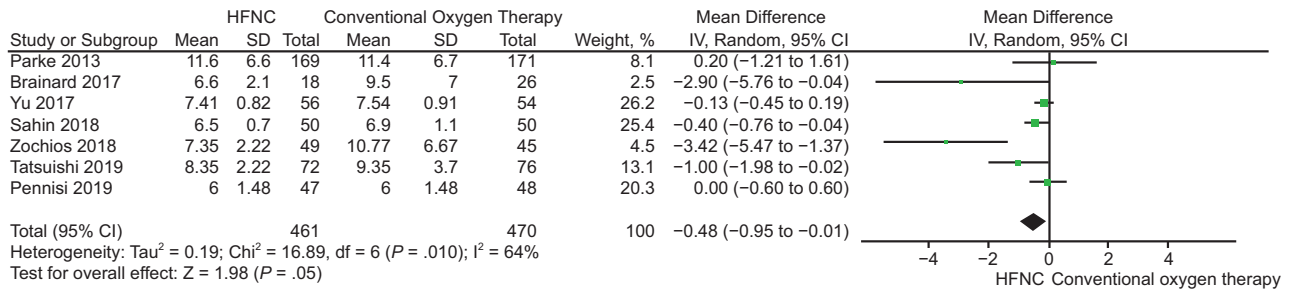


Fig. 4. Hospital stay. HFNC = high-flow nasal cannula; IV = inverse variance.

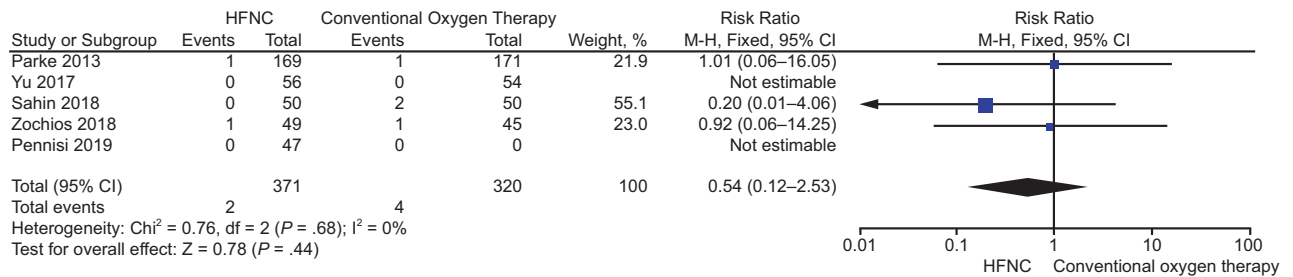


Fig. 5. Hospital mortality. HFNC = high-flow nasal cannula; M-H = Mantel-Haenszel.

was also associated with delayed intubation and poor prognosis in subjects with acute respiratory failure.<sup>33,34</sup> One previous study reported that HFNC could reduce the risk of re-intubation compared with conventional oxygen therapy among extubated subjects at low risk for re-intubation.<sup>35</sup> Moreover, a recent meta-analysis of randomized controlled trials reported that HFNC might not delay re-intubation and could be the first-line therapy in postoperative patients without acute respiratory failure.<sup>36</sup> For these reasons, HFNC is safe and effective among patients undergoing cardiothoracic surgery. Another finding of our meta-analysis is the shorter length of hospital stay for the HFNC group compared to that for the conventional oxygen therapy group. The length of hospital stay is affected by multiple factors, and we should be cautious about explaining this result due to the significant heterogeneity ( $I^2 = 64%$ ). Studies have reported that re-intubation is associated with higher mortality, prolonged duration of mechanical ventilation, and higher hospital costs.<sup>37</sup> We observed a significant reduction in re-intubation rates in the HFNC group, which may be the main reason for the probable reduction in hospitalization rates. One study reported that reduced FEV<sub>1</sub> was associated with increased hospital stay following cardiac surgery.<sup>38</sup> However, none of the studies comparing HFNC with conventional oxygen therapy during and after cardiothoracic surgery reported differences in FEV<sub>1</sub> before and after surgery between groups.<sup>20,21,39</sup> More studies are needed to confirm the relationship between air-flow limitation and length of hospital stay in

patients undergoing cardiothoracic surgery. In addition, the criteria for discharge from the hospital were not identical among different medical centers, which might lead to an insignificant difference in the stay between the groups.

Cardiothoracic patients are usually transferred to the ICU after surgery. They are extubated and receive noninvasive oxygen therapy for a short period of time in the ICU before transferring back to the general ward. Our review did not identify a difference between the 2 groups in terms of length of ICU stay, and because this period includes both invasive mechanical ventilation and noninvasive oxygen therapy, it may not be a good indicator to evaluate the effect of HFNC and conventional oxygen therapy. In addition, no significant differences were found for the incidence of pulmonary complications or mortality. A previous meta-analysis on this topic defined pulmonary complications as atelectasis, pneumonia, hypoxemia, and hypercapnia and noted significant differences between HFNC and conventional oxygen therapy based on only 2 studies.<sup>40</sup> In our study, pulmonary complications were defined as pneumonia and atelectasis based on the majority of complications reported in the articles we included. HFNC could provide PEEP of 3–5 cm H<sub>2</sub>O at flows of 30–50 L/min to increase alveolar recruitment and improve oxygenation.<sup>41</sup> These pulmonary complications may be related to the general condition of patients before operations, pathological and physiological compensatory reactions after operations, treatments, nursing, etc. In

addition, the sample size was relatively small, and the incidence of pulmonary complications (10.5% for HFNC vs 12.4% for conventional oxygen therapy) and death rate (0.54% for HFNC vs 1.25% for conventional oxygen therapy) were quite low. As a result, it is possible that our study was not sufficiently powered to elucidate the effects of HFNC on mortality. Some previous studies have drawn conclusions similar to ours. Leeies et al<sup>42</sup> reported that there was no significant difference in mortality between the HFNC group and the standard oxygen therapy group among subjects with acute respiratory failure. Furthermore, it has been reported that, compared with conventional oxygen therapy, HFNC did not improve pulmonary outcomes (eg, the occurrence of hypoxemia, pulmonary complications, and mortality) among subjects undergoing major abdominal surgery.<sup>43</sup> Based on the available studies, use of HFNC after extubation of cardiothoracic surgery patients may not reduce pulmonary complications and mortality compared to conventional oxygen therapy.

To our knowledge, this is the largest meta-analysis comparing HFNC with conventional oxygen therapy for postcardiothoracic surgery subjects. Two meta-analyses previously explored the effect of HFNC versus conventional oxygen therapy on adults after cardiothoracic surgery. Zhu et al<sup>40</sup> included only 2 studies and stated that HFNC significantly reduced the rate of the escalation of respiratory support but not the rate of re-intubation compared with conventional oxygen therapy. This conclusion was confirmed by a meta-analysis of 4 studies, which also reported that HFNC significantly reduced the incidence of pulmonary complications.<sup>44</sup> However, the results of our meta-analysis were not identical to these 2 meta-analyses. Our meta-analysis included 8 randomized controlled trials and a larger sample size. We further confirmed that HFNC significantly reduced the need to escalate respiratory support. In addition, the biggest difference from the previous meta-analysis was the finding that HFNC significantly reduced the re-intubation rate and possibly the length of hospital stay. These findings may provide more clinical evidence for the choice of HFNC for such patients.

There are some limitations that need to be noted. First, clinical heterogeneity of the interventions is inevitable. The uneven distribution of underlying diseases, criteria for the escalation of respiratory support, and oxygen therapy parameters will affect the evaluation of HFNC. Second, the studies included in our meta-analysis were all published in English, which suggests that some potentially related studies might not have been included because of language restrictions. Finally, our study included only 8 articles, and more high-quality studies are needed to further confirm the efficacy of HFNC.

## Conclusions

HFNC significantly reduced the need for the escalation of respiratory support and the re-intubation rate, and it might reduce the hospital stay as well. HFNC can be safely administered after extubation for adult patients undergoing cardiothoracic surgery. More high-quality randomized controlled trials are needed to further validate our results.

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