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The Effect of High-Flow Nasal Oxygen Therapy on Postoperative Pulmonary Complications and Hospital Length of Stay in Postoperative Patients: A Systematic Review and Meta-Analysis

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Abstract

Objective: To evaluate the effect of high-flow nasal cannula oxygen (HFNO) therapy on hospital length of stay (LOS) and postoperative pulmonary complications (PPCs) in adult postoperative patients. **Data Sources:** PubMed, Embase, the Cochrane Library, Web of Science of Studies, China National Knowledge Index, and Wan Fang databases were searched until July 2018. **Study Selection:** Randomized controlled trials (RCTs) comparing HFNO with conventional oxygen therapy or noninvasive mechanical ventilation in adult postoperative patients were included. The primary outcomes were hospital LOS and PPCs; short-term mortality (defined as intensive care unit, hospital, or 28-day mortality) and intubation rate were the secondary outcomes. **Data Extraction:** Demographic variables, high-flow oxygen therapy application, effects, and side effects were retrieved. Data were analyzed by the methods recommended by the Cochrane Collaboration. The strength of evidence was assessed by the Grading of Recommendations Assessment, Development and Evaluation. Random errors were evaluated with trial sequential analysis. **Data Synthesis:** Fourteen studies (2568 patients) met the inclusion criteria and were included. Compared to the control group, the pooled effect showed that HFNO was significantly associated with a shorter hospital stay (mean difference: −0.81; 95% confidence interval [CI]: −1.34 to −0.29, $P = .002$), but not mortality (risk ratio [RR]: 1.0, 95% CI: 0.63 to 1.59, $P = 1.0$). Weak evidence of a reduction in reintubation rate (RR: 0.76, 95% CI: 0.57-1.01, $P = .06$) and PPC rate (RR: 0.89, 95% CI: 0.75-1.06, $P = .18$) with HFNO versus control group was recorded. **Conclusions:** The available RCTs suggest that, among the adult postoperative patients, HFNO therapy compared to the control group significantly reduces hospital LOS.

Keywords

high-flow oxygen therapy, length of stay, postoperative pulmonary complications, reintubation, mortality

Introduction

Surgical volume is growing every year; Weiser's data suggested that up to 312.9 million operations took place from 194 Member States of the World Health Organization in 2012.[1] Patients undergoing major surgery are at significant risk for the development of respiratory failure which was mainly caused by complications (postoperative pulmonary complications [PPCs]), diaphragmatic dysfunction, and other nonrespiratory factors.[2-4] Postoperative pulmonary complications are associated with prolonging hospital length of stay (LOS), increased intubate rate, and high mortality and costs.[5-7] When conventional oxygen therapy (COT) is insufficient to correct hypoxemia and provide adequate humidification, noninvasive ventilation (NIV) has emerged as a successful strategy to avoid reintubation and improve outcomes, notably as a preventive or curative intervention after surgery.[8-10] However, NIV has important limitations,[11-13] which is difficult to implement in wards other than special resources such as intensive care unit (ICU), respiratory department, and emergency department, and

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it may cause patient discomfort for prevention of normal oral intake, less effective clearance of secretions, and prevention of usual communication with others.

High-flow nasal cannula oxygen (HFNO) is a new technique that involves the continuous delivery of up to 60 L/min and delivers up to 100% humidified oxygen. It is increasingly used because of its advantages including ease of application, patient tolerance, providing a certain level of positive end-expiratory pressure (PEEP) to improve alveolar recruitment, and enhanced washout of nasopharyngeal dead space.[14-16]

Many studies have shown that, compared to COT or NIV, HFNO in postextubation nonsurgical patients could decrease ICU LOS, intubation rate and improve respiratory parameters, comfort, and patient tolerance.[17-19] Recently, several uncontrolled, prospective studies,[20,21] randomized controlled trials (RCTs),[7,13,22-30] and an early meta-analysis[31] have examined its use to postoperative patients. Most of these RCTs reduced the trend of hospital LOS, but lack statistical significance; meanwhile, HFNO had an inconsistent effect on intubation rate and mortality. In light of new evidence and with the aid of increased power of meta-analytic techniques, we perform a systematic review and meta-analysis of the literature to compare the effect of HFNO with other respiratory support techniques on the primary outcomes of hospital LOS and PPCs and the secondary outcome including short-term mortality and intubation rate in postoperative patients.

Methods

This meta-analysis is based on previously published studies, so ethical approval and patient consent is not required.

Study Selection

Two authors (Z.-H.L. and W.C.) assessed titles and abstracts independently to determine whether a study met the inclusion criteria. Then all trials were independently reviewed according to the inclusion and exclusion criteria. Any differences are resolved by consensus on the inclusion or exclusion of a particular study after a discussion with the third reviewer (S.-S.M.).

Data Sources and Searches

We searched PubMed, Embase, the Cochrane Library, Web of Science of Studies, China National Knowledge Index, and Wan Fang databases from inception to July 31, 2018, with the following search terms: (“high flow” or “high-flow”) and (“operation” or “operative” or “surgery” or “surgical”) limited to RCTs. No limits for the location of the original study, gender, sample size, or language were entered for the search.

Inclusion Criteria

To determine which publications were suitable for the meta-analysis, we used the following selection criteria: (1) RCTs; (2) study population was adult postoperative patients; (3) use of HFNO compared to control strategy (COT or NIV); (4) studies included should report at least one of the predefined outcomes: hospital LOS, PPCs (we defined PPC as at least one of the following 3: atelectasis, pneumonia, or PPC), reintubation rate, and mortality (we defined mortality as ICU or hospital or 28-day mortality; if a study reported all of these outcome measures, the longest observation period was preferred).

Exclusion Criteria

Exclusion criteria were as follows: (1) without control group; (2) the study was a review, letter, case report, or other type of publication not based on original research; and (3) in vitro study or animal experiments.

Data Extraction

Two reviewers (M.X. and Z.-H.L.) undertook an initial relevance screen of the titles and abstracts of identified studies for potential eligibility. Any disagreements between the 2 investigators were resolved by discussion and consensus with the third one (W.C.).

Subgroup Analysis

For the primary and secondary outcomes, we performed the following a priori subgroup analyses: patients with different type of surgery (cardiac, thoracic, and abdominal surgery) and different risks of reintubation (high risk or low risk: the average values of risk-related parameters for reintubation were assessed according to Hernandez’s trials),[17,18] maintaining the different target SPO_2 (90%-93% and 95%) and strategy (prophylactic, therapy).

Assessment of Risk of Bias

Internal validity of the included studies was assessed according to the Cochrane Collaboration methodology,[32] which consists of the following domains: adequacy of sequence generation, allocation sequence concealment, blinding of participants and caregivers, blinding for outcome assessment, incomplete outcome data, selective outcome reporting, and the other sources of bias.

Grading the Evidence

We graded the strength of evidence by applying the GRADE levels (high, moderate, low, and very low) by evaluating design, quality, consistency, precision, directness, and possible publication bias of the included trials using GRADEpro Guideline Development Tool.[33]

Data Synthesis and Analysis

We used Review Manager Software (The Nordic Cochrane Center, The Cochrane Collaboration, Copenhagen Denmark) for the meta-analysis, which provide the risk ratio (RR) with

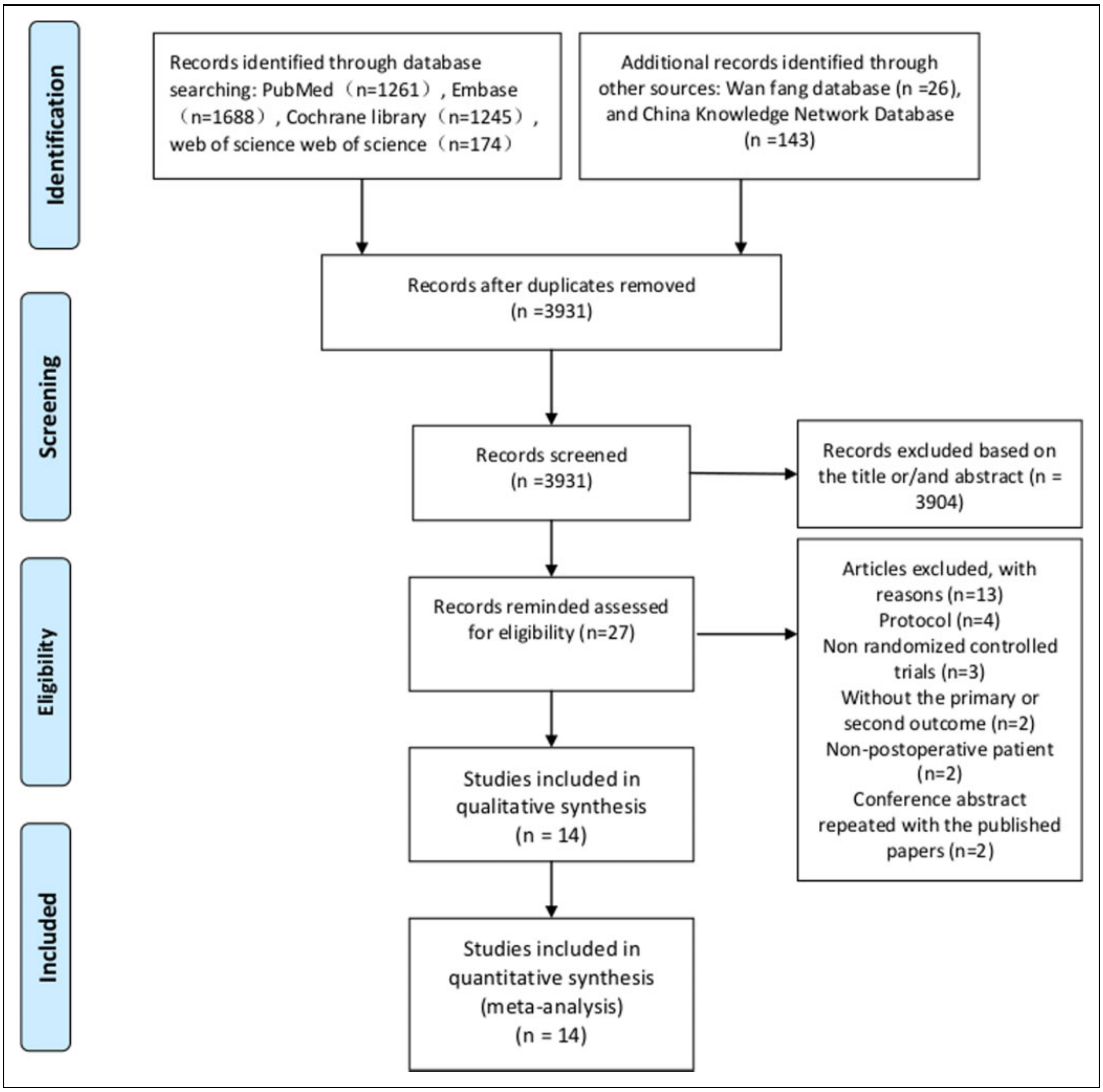

Figure 1. Flow diagram (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) of trial selection.

95% confidence intervals (CIs) for primary and secondary outcomes. The mean and standard deviation were estimated based on the median and quartiles of the hypothetical normal distribution data. The statistical heterogeneity was measured and quantified by χ^2 test and the *I*2 test. In addition, I^2 index was used to assess heterogeneity in the meta-analysis with 25%, 50%, and 75% of I^2 values meaning low, medium, and high heterogeneity, respectively, proposed by Higgins and colleagues.[34] If the data heterogeneity is obvious ($I^2 > 50\%$), we used the random-effects model; otherwise, a fixed-effects model was applied. Publication bias was evaluated by visual inspection of funnel plots. We considered a *P* value less than .05 as statistically significant.

Due to type I errors which result from an increased risk of random error and repeated significance testing, we used trial sequential analysis (TSA; TSA software version 0.9 Beta; Copenhagen Trial Unit, Copenhagen, Denmark), which estimated the amount of information with an adjusted threshold for statistical significance in the cumulative meta-analysis.

Results

Search Results and Trial Characteristics

The selection process for the eligible studies is shown in Figure 1. Firstly, 4537 potentially relevant records were identified and 606 were excluded after duplicate records were removed. Secondly, the titles and abstracts were screened for the terms “high flow,” “oxygen,” and “surgery or the other operation”; 27 studies were remained for assessment. Finally, after searching and reading all text articles, 14 studies were included in the present meta-analysis. A total of 2568 patients were included in 14 trials; of which, 1285 patients were the randomly assigned to HFNO group and 1283 to the control group. The main characteristics of the included studies are shown in Table 1. The

Table 1. Populations and Interventions in Studies of Oxygen Therapy in Postoperative Adults.[a]

Study	No. Studies (No. of Patients)	Control Group	Type of Surgery	Age	Min Target SPO_2 (%)	Risk of Reintubation	Strategy
Brainard et al, 2017	44	COT	Thoracic	57 (14)/59 (16)	95	NA	Prophylactic
Geng et al, 2017	48	COT	Mix	63 (50 to 68)	90	High	Therapy
Sun et al, 2017	48	COT	Thoracic	66.7 (2.4)	100	High	Therapy
Yu et al, 2017	110	COT	Thoracic	56.31 (7.03)/55.82 (7.92)	95	High	Prophylactic
Futier et al, 2016	220	COT	Abdominal or combine thoracic	62 (12)/61 (13)	95	NA	Prophylactic
Corley et al, 2015	155	COT	Cardiovascular	63 (11.4)/65 (11.1)	95	High	Prophylactic
Parke et al, 2013	340	COT	Cardiovascular	65 (19-88)/66 (21-87)	93	High	Prophylactic
Bickel et al, 2011	210	COT	Abdominal	28.5 (12.3)/27.6 (10.8)	NA	NA	Prophylactic
Stéphan et al, 2015	830	NIV	Cardiovascular	63.9 (62.6-65.2)/63.8 (62.5-65.2)	92	NA	Therapy
Ansari et al, 2015	59	COT	Thoracic	68.3 (8.5)/65.7 (13.0)	93	High	Prophylactic
Yang et al, 2017	40	NIV	Cardiovascular	53.8 (8.9)/52.8 (7.9)	P/F 200	NA	Therapy
Blaudszun et al, 2017	99	COT	Cardiovascular	NA	NA	High	Prophylactic
Stéphan et al, 2017	271	NIV	Cardiovascular	63.4 (11.8)/64.5 (11.3)	92	NA	Therapy
Zochios et al, 2018	94	COT	Cardiovascular	67.3 (9.3)/69.1 (11.1)	95	High	Prophylactic

Abbreviations: COT, conventional oxygen therapy; NA, not available; NIV, noninvasive mechanical ventilation.
[a]Data are expressed as median (interquartile range), or mean (standard deviation).

studies were published between 2011 and 2018 with 7 cardiac surgery,[7,13,24,26,28,29,35] 4 thoracic surgery,[22,25,30,36] 2 abdominal surgery,[23,27] and 1 other surgery.[37]

Risk of Bias and Random Errors in the Included Studies

The risk of bias for each article was evaluated and the details of the results are presented in Figure 2A. Because blinding of patients and caregivers was impossible in these trials, so it might lead to performance bias.

Trial sequential analysis was calculated with $\alpha = 0.05$ and $\beta = 0.20$ (power 80%) and a required diversity-adjusted information size based on the intervention effect suggested by the included trials using a random-effects model (mean difference [MD] of -0.75 regarding hospital LOS and 4265 patients). Trial sequential analysis indicates sufficient reliable and conclusive evidence that HFNO is beneficial to hospital LOS (Figure 2B), since the monitoring boundaries were finally surpassed and the required information size was reached.

Outcomes Analyses

Twelve studies reported the data of hospital LOS. A total of 1180 patients treated with HFNO and 1185 patients received non-HFNO. The hospital LOS in the HFNO group was significantly lower than the control group (MD -0.81; 95% CI: -1.34 to -0.29, $P = .002$) with heterogeneity ($I^2 = 58\%$; Figure 3A). Funnel plots suggest that there may be publication bias in Blaudszun's research from the meta-analysis of hospital LOS (Online supplemental Figure S1). However, we graded the overall strength of the evidence as low (Table 2), which means that further research may change the estimate. The findings of the subgroup analyses for the primary outcome of hospital LOS, according to type of surgery, min-target SPO_2, risk of reintubation, and therapy strategy, are summarized in Table 3. For these outcomes, most subgroup analyses did not change significantly and have similar results or trends (Table 3).

Postoperative pulmonary complications were reported in 7 trials including 775 patients treated with HFNO and 788 patients with non-HFNO. Weak evidence of a reduction in PPCs (RR: 0.89, 95% CI: 0.75-1.06, $P = .18$, $I^2 = 0\%$) with HFNO group versus control group was recorded (Figure 3B). We graded the overall strength of the evidence as moderate (Table 2). Subgroup analysis showed that the incidence of PPCs had a downward trend in min-target SPO_2 95% group and prophylactic group and similar result also appeared in comparison with COT (Table 3).

Reintubation rate was reported in 9 trials with no obvious publication bias. Of the 942 patients treated with HFNO, 68 (7.54%) were intubated compared to 86 (9.96%) of 944 receiving non-HFNO. A downward trend in intubation rate was found in the HFNO group (RR: 0.76, 95% CI: 0.57-1.01, $P = .06$, $I^2 = 40\%$; Figure 4A). We graded the overall strength of the evidence as low (Table 2), which means the further research will likely change the estimate. Subgroup analysis showed similar results in thoracic surgery group min-target SPO_2 95% group, prophylactic group, therapy group, and had a downward trend in comparison with COT group (Table 3). Subgroup also showed that HFNO significantly decreased the PPC rate in patients with min-target SPO_2 95% (RR: 0.33, 95% CI: 0.14-0.79, $P = .01$, $I^2 = 0\%$) and high risk of reintubation (RR: 0.29, 95% CI: 0.13-0.62, $P = .001$, $I^2 = 26\%$; Table 3).

Mortality was reported in 6 trials. Of the 931 patients treated with HFNO, 35 (3.76%) were intubated compared to 36 (3.85%) of 934 receiving non-HFNO. No significant difference in mortality was found between the 2 groups (RR: 1.0, 95% CI:

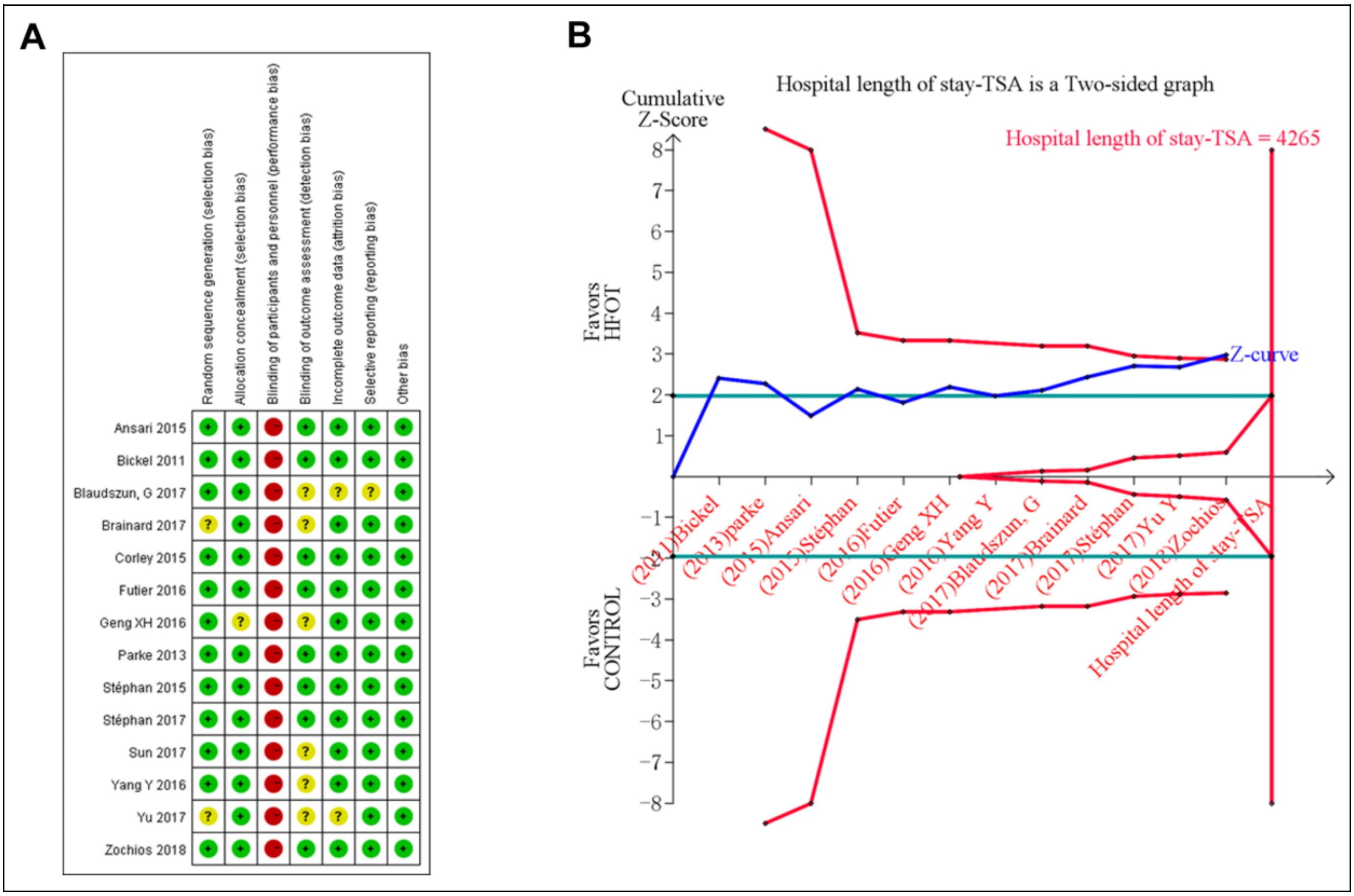

Figure 2. A, Risk of bias summary for each included study. Red (–) indicates high risk of bias; yellow (?) indicates unclear risk; and green (+) indicates low risk of bias. B, Trial sequential analysis for mean difference reduction of hospital stay in postoperative patients.

0.63-1.59, $P = 1.0$, $I^2 = 0\%$; Figure 4B). We graded the overall strength of the evidence as moderate (Table 2). There were no significant changes in the outcome of subgroup analysis of mortality based on the type of surgery, minimum target SPO_2, reintubation risk, and treatment strategy (Table 1).

Discussion

In the current meta-analysis of RCTs, we reviewed the literature on the efficacy of HFNO in postoperative patients. The pooled results of the included 14 studies showed that: (1) HFNO was associated with shorter hospital LOS of postoperative patients compared to the control group confirmed by TSA. (2) The trends of reduced PPCs and reintubation rate were found in postoperative patients treated with HFNO. (3) High-flow nasal cannula oxygen did not reduce mortality. (4) High-flow nasal cannula oxygen group had significantly lower intubation rate of patients compared to the COT group, and it also reduced intubation rates in high-risk patients.

In efforts to optimize the postoperative treatment strategies after surgeries, clinicians need to decide the further oxygen therapy based on which method is more effective in preventing PPCs that may increase hospital LOS, morbidity, mortality,[38] and costs for the health care.[39] High-flow oxygen therapy, by providing PEEP support over COT, without discomfort of NIV artificial mask,[40] offers a potential solution to the PPCs. Clinicians might still be reluctant to adopt the HFNO approach to preventing PPC for the postoperative patients because PEEP offered by HFNO, which is easily affected by the patient's mouth state and the other factors,[16,41] may not provide a more stable positive pressure than NIV. So the optimal choice for preventing PPC of noninvasive respiratory support remains to be determined.

Although the results from this meta-analysis are encouraging, several important issues deserve a detailed discussion. The primary outcome in our meta-analysis or subgroup analysis (HFNO vs COT) is inconsistent with previous meta-analyses[42] on the topic, but the meta-analysis showed that using HFNO did not reduce hospital LOS compared to COT. The reason may be different patient populations (postoperative patients, non-postoperative patients) included, so that neutral results and significant heterogeneity were seen in the meta-analysis (I^2 up to 97%). In addition, insufficient sample size may be another reason for the inconsistence. Although our primary result is moderate heterogeneous, they still appear to be robust because most of the results are consistent when

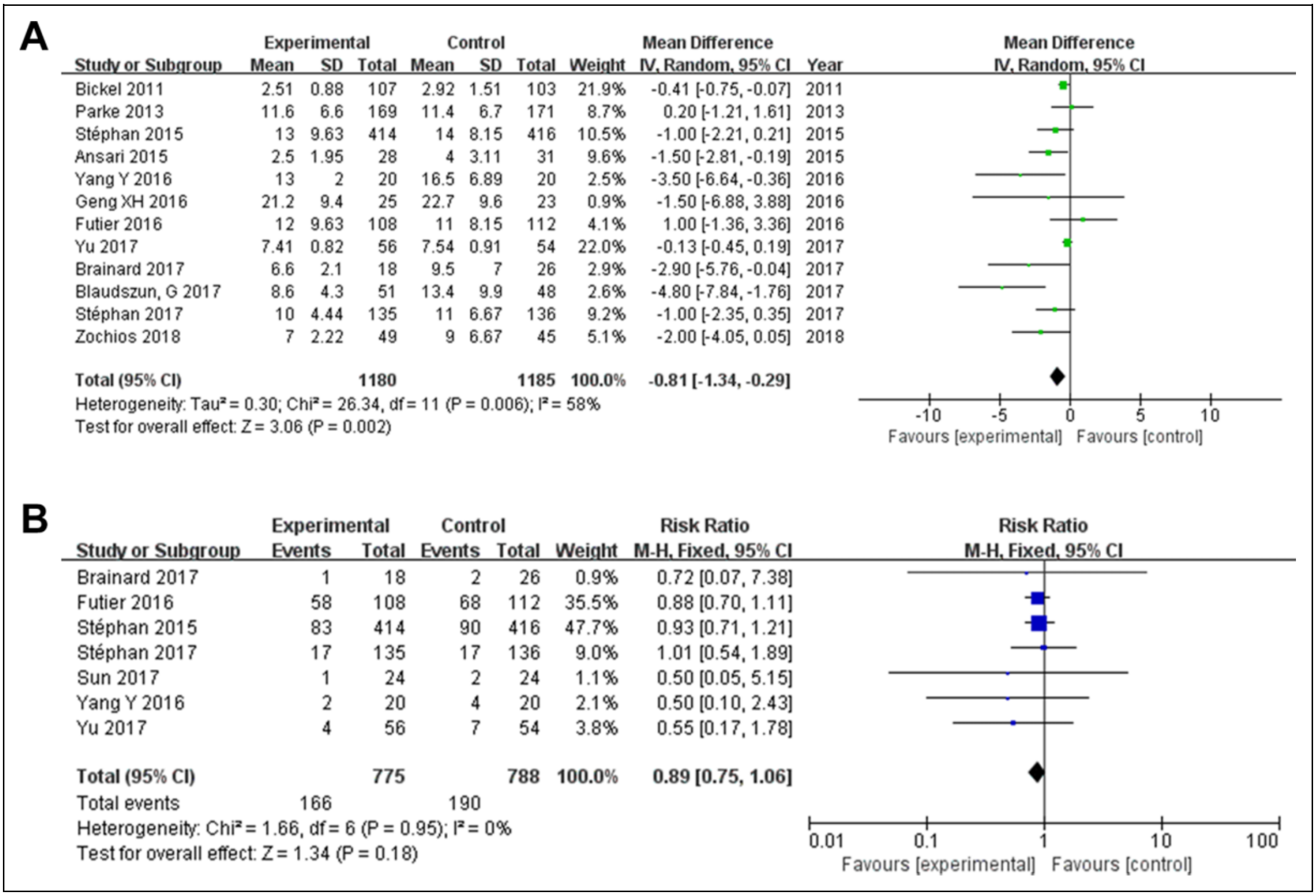

Figure 3. A, Hospital stay of the high-flow nasal cannula oxygen therapy (HFNO) and control groups. B, Reintubation rate of the high-flow nasal cannula oxygen therapy (HFNO) and control groups.

performing subsequent subgroup analyses. Our sensitivity analyses and funnel plot showed the heterogeneity is mainly derived from the study of Blaudszun.[24] Because the study is a conference abstract and the data provided are limited, it is difficult to find the cause of the heterogeneity. But after excluding this trial, the pooled result of the remaining studies turned into mild heterogeneity and did not change the original analysis results. Similar findings have appeared in another high-quality RCT that is included in medical and surgical patients (interquartile range [IQR]: HFNO group 11 days and COT 12 days).[18]

Many studies have showed that the duration of postoperative hospital stay and longer hospital stay were recorded in patients with PPCs.[43] We also observed that a downward intend in hospital LOS in the HFNO group decreased in parallel with the incidence of PPC. Studies have shown that lowering the incidence of PPC was associated with shorter hospital stay, reduction rate of reintubation, and mortality,[5,6,44,45] but the effect of HFNO on PPCs has been controversial,[46] and the current meta-analysis result indicates that HFNO had a positive effect on the reduction in PPC and shorting hospital LOS, but the overall strength of the evidence graded was low and we may still require a larger sample size and a better quality RCT to confirm.

Prior to this, meta-results on HFNO applied to postoperative patients showed that HFNO could not reduce the rate of reintubation compared to COT, but its limitation was a small sample size (n = 495), and the patients were from cardiac surgery.[31] The current meta-analysis expands the sample size of postoperative patients with reintubation data (n = 1886) and the analysis results obtained suggested that HFNO may contribute to the reduction intend of intubation rate, but still need further research to confirm. However, HFNO reduced the intubation rate of thoracic surgical patients and it also decreased it compared to the COT group, which may be due to washout of nasopharyngeal dead space, decreasing work of breathing, regulating the inhaled gas affecting the physiological response of the lungs, and providing expansion pressure of 2 to 5 cm H_2O.[47]

Recently, reintubation risk becomes a useful variable for assessing whether a patient is prone to respiratory failure. High-flow nasal cannula oxygen was not inferior to noninvasive mechanical ventilation for preventing reintubation among high-risk intubation population[17] and reduced the risk of reintubation compared to COT among low-risk intubation population.[18] Accordingly, we set the high risk intubation on the basis of the average values provided by all RCTs and made a subgroup analysis.[17] The results were that HFNO could decrease

Table 2. GRADE Evidence Profile for the Studies in the Meta-Analysis.

Quality Assessment							No. Patients		Effect			
No. Studies	Design	Risk of Bias	Inconsistency	Indirectness	Imprecision	Other Considerations	HFNO	Control	Relative (95% CI)	Absolute	Quality	Importance
Hospital stay (better indicated by lower values)												
12	Randomized trials	No serious risk of bias	Serious[a]	No serious indirectness	No serious imprecision	Reporting bias[b]	1180	1185	–	MD 0.81 lower (1.34-0.29 lower)	⊕⊕OO Low	Critical
Quality Assessment							No. patients		Effect			
No. Studies	Design	Risk of Bias	Inconsistency	Indirectness	Imprecision	Other Considerations	PPC	Control	Relative (95% CI)	Absolute	Quality	Importance
PPC												
7	Randomized trials	No serious risk of bias	No serious inconsistency	No serious indirectness	Serious[c]	None	166/775 (21.4%)	190/788 (24.1%)	RR 0.89 (0.75-1.06)	27 fewer per 1000 (from 60 fewer to 14 more)	⊕⊕⊕O Moderate	Critical
								13%		14 fewer per 1000 (from 32 fewer to 8 more)		
Quality Assessment							No. Patients		Effect			
No. Studies	Design	Risk of Bias	Inconsistency	Indirectness	Imprecision	Other Considerations	Reintubation	Control	Relative (95% CI)	Absolute	Quality	Importance
Reintubation												
9	Randomized trials	No serious risk of bias	Serious[d]	No serious indirectness	Serious[e]	None	71/942 (7.5%)	94/944 (10%)	RR 0.76 (0.57-1.01)	24 fewer per 1000 (from 43 fewer to 1 more)	⊕⊕OOLow	Critical
								9.3%		22 fewer per 1000 (from 40 fewer to 1 more)		
Quality Assessment							No. Patients		Effect			
No of Studies	Design	Risk of Bias	Inconsistency	Indirectness	Imprecision	Other Considerations	Mortality	Control	Relative (95% CI)	Absolute	Quality	Importance
Mortality												
6	Randomized trials	No serious risk of bias	No serious inconsistency	No serious indirectness	Serious[f]	None	35/931 (3.8%)	36/934 (3.9%)	RR 1 (0.63-1.59)	0 fewer per 1000 (from 14 fewer to 23 more)	⊕⊕⊕O Moderate	Critical
								2.5%		0 fewer per 1000 (from 9 fewer to 15 more)		

Abbreviations: CI, confidence interval; HFNO, high-flow nasal cannula oxygen; MD, mean difference; PPC, postoperative pulmonary complications; RR, risk ratio.
[a] $I^2 = 58\%$, the heterogeneity was moderate.
[b] Funnel plots suggest that there may be publication bias in Blaudszun research.
[c] The confidence intervals of the pooled RR slightly crossed the line of no effect.
[d] $I^2 = 40\%$, the heterogeneity was mild.
[e] The confidence intervals of the pooled RR slightly crossed the line of no effect.
[f] The of the pooled confidence intervals RR slightly crossed the line of no effect.

Table 3. Summary Estimates of Effect of High-Flow Oxygen Therapy in Postoperative Adults.

Outcome	No. Studies (No. Patients)	Summary Estimate (95% CI)	*P* Value (Summary Estimate)	*P* Value (Heterogeneity)	I^2 (%)
Length of stay in hospital	12 (2365)	−0.81[a] (−1.34 to −0.29)	.002	.006	58
Cardiac surgery	6 (1674)	−1.50[a] (−2.64 to −0.36)	.01	.04	58
Thoracic surgery	3 (213)	−1.06[a] (−2.48 to 0.35)	.14	.03	73
Abdominal surgery	2 (430)	−0.38[a] (−0.71 to −0.05)	.02	.25	26
HFNO vs NIV	3 (1141)	−1.19[a] (−2.16 to −0.32)	.007	.33	11
HFNO vs COT	9 (1224)	−0.67[a] (−1.26 to −0.09)	.02	.008	61
Min target SPO_2 (90%-93%)	5 (1548)	−0.88[a] (−1.53 to −0.22)	.009	.52	0
Min target SPO_2 (95%)	5 (509)	−1.17[a] (−2.63 to 0.30)	.12	.02	66
Prophylactic	8 (1176)	−0.68[a] (−1.27 to −0.08)	.03	.005	66
Therapy	4 (1189)	−1.20[a] (−2.05 to −0.34)	.006	.52	0
High risk of reintubation	6 (750)	−1.13[a] (−2.25 to −0.01)	.05	.007	65
PPCs	7 (1563)	0.89[b] (0.75 to 1.06)	.18	.95	0
Cardiac surgery	4 (1189)	0.92[b] (0.72 to 1.16)	.47	.82	0
Thoracic surgery	2 (154)	0.58[b] (0.21 to 1.66)	.31	.84	0
HFNO vs NIV	3 (1141)	0.92[b] (0.73 to 1.18)	.52	.72	31
HFNO vs COT	4 (422)	0.84[b] (0.67 to 1.06)	.14	.83	0
Min target SPO_2 (90%-93%)	4 (414)	0.83[b] (0.66 to 1.05)	.12	.76	0
Min target SPO_2 (95%)	3 (1149)	0.93[b] (0.73 to 1.19)	.57	.85	0
Prophylactic	3 (374)	0.85[b] (0.67 to 1.07)	.17	.72	0
Therapy	4 (1189)	0.92[b] (0.72 to 1.16)	.47	.82	0
High risk of reintubation	2 (88)	0.50[b] (0.13 to 1.85)	.30	1.00	0
Intubation	9 (1886)	0.76[b] (0.57 to 1.01)	.06	.10	40
Cardiac surgery	5 (1636)	0.95[b] (0.69 to 1.25)	.73	.42	0
Thoracic surgery	3 (202)	0.31[b] (0.12 to 0.81)	.02	.51	0
HFNO vs NIV	3 (1141)	0.95[b] (0.69 to 1.30)	.73	.45	0
HFNO vs COT	4 (745)	0.31[b] (0.15 to 0.64)	.002	.31	16
Min target SPO_2 (90%-93%)	4 (1489)	0.71[b] (0.28 to 1.80)	.47	.08	56
Min target SPO_2 (95%)	3 (397)	0.33[b] (0.14 to 0.79)	.01	.82	0
Prophylactic	4 (649)	0.45[b] (0.15 to 1.32)	.15	.24	29
Therapy	5 (1237)	0.54[b] (0.26 to 1.12)	.10	.08	53
High risk of reintubation	5 (701)	0.29[b] (0.13 to 0.62)	.001	.25	26
Mortality	6 (1865)	1.00[b] (0.63 to 1.59)	1.00	.58	0
Cardiac surgery	4 (1535)	1.00[b] (0.63 to 1.60)	.99	.44	0
HFNO vs NIV	2 (1101)	0.79[b] (0.26 to 2.42)	.69	.10	63
HFNO vs COT	4 (764)	0.80[b] (0.22 to 2.96)	.74	.97	0
Min target SPO_2 (90%-93%)	3 (1441)	1.01[b] (0.62 to 1.62)	.98	.26	25
Min target SPO_2 (95%)	3 (424)	0.75[b] (0.17 to 3.31)	.70	.86	0
Prophylactic	4 (764)	0.80[b] (0.22 to 2.96)	.74	.97	0
Therapy	2 (1101)	0.79[b] (0.26 to 2.42)	.69	.10	63
High risk of reintubation	5 (544)	0.96[b] (0.14 to 6.75)	.97	.96	0

Abbreviations: COT, conventional oxygen therapy; HFNO, high-flow oxygen therapy; NIV, noninvasive mechanical ventilation; PPCs, postoperative pulmonary complications.
[a] Weighted mean difference.
[b] Relative risk.

reintubation rate and hospital stay in high-risk intubation postoperative patients. However, it was not associated with lower PPC rate and hospital mortality, which might be affected by the limited number of RCTs. It should be noted that since our observations regarding risk of reintubation are according to the provided average value, conclusions regarding the relative effectiveness of HFNO in subgroups of patients would be misleading. Nonetheless, we are able to generate hypotheses that may be tested by future trials.

Recent studies reported that among critically ill patients, conservative oxygen therapy (with a slightly lower SPO_2 target) versus conventional therapy resulted in lower mechanical ventilation time, hospital mortality, or ICU mortality.[48,49] This meta-analysis showed that HFNO reduced the intubation rate while maintaining SPO_2 above 95% but not 90% to 93%; there was an opposite gradient in PPC reduction according to SPO_2 target, with SPO_2 90% to 93%, then SPO_2 95%. Therefore, we speculate that HFNO may improve other factors affecting respiration (eg, sepsis, diabetes mellitus needing insulin therapy, active congestive heart failure, hypertension requiring medication, chronic obstructive pulmonary disease, low preoperative functional status),[50,51] not just PPC to reduce

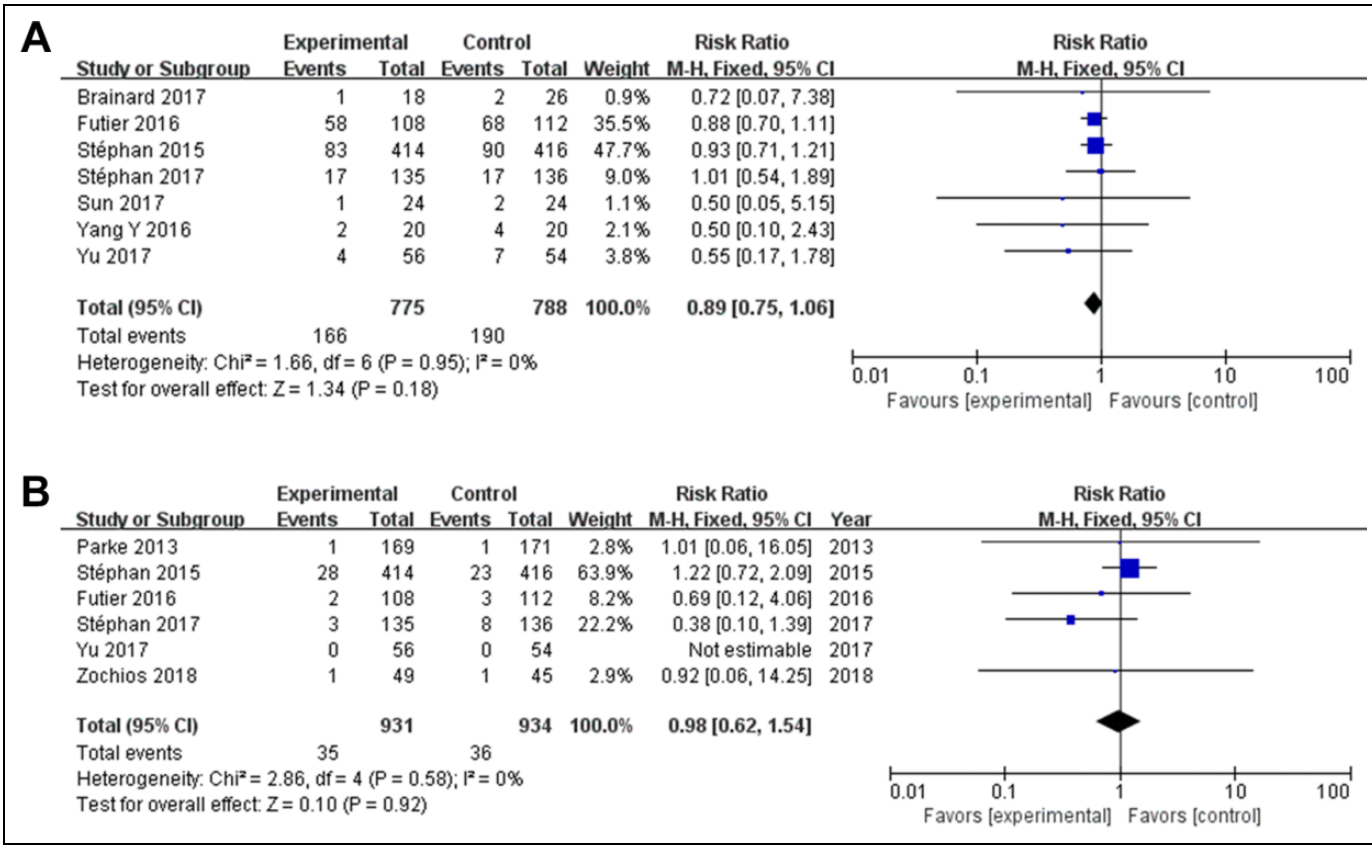

Figure 4. A, Postoperative pulmonary complication rate of the high-flow nasal cannula oxygen therapy (HFNO) and control groups. B, Mortality of the high-flow nasal cannula oxygen therapy (HFNO) and control groups.

intubation rate. Future RCTs on the application of HFNO in postoperative patients need to consider the exclusion of non-respiratory causes on reintubation and hospital stay.

Both PPC and reintubation are associated with increased patient mortality.[52,53] Although both of them showed a downward trend in the HFNO group compared to the control group in the meta-analysis, HFNO failed to affect mortality. Mortality may not be the primary end point of the meta-analysis which may lead to biases and affect the results.

Finally, to the best of our knowledge, this is the first meta-analysis to assess the efficacy of HFNO as a technique in hospital LOS of postoperative patients. However, our study also has some limitations. Firstly, most of the studies included in this meta-analysis are single-center studies that may lead to bias,7,22,23,25,26,28,35-37 as single-centre clinical trials with continuous outcomes may show slightly larger intervention effects than did multicenter trials.[54] Secondly, the risk of PPCs may be different in the included studies, which may lead to biased results. According to the Assess Respiratory Risk in Surgical Patients in Catalonia (ARISCAT) score for PPCs, we found that the intrathoracic incision score (24 points) was given higher score than abdomen (15 points). In addition, age may be another important factor affecting the incidence of PPCs and the data included in this meta-analysis showed that the average age is from 28 to 68 years old. However, due to the limited data available in the studies, we were unable to perform a stratified analysis based on ARISCAT score. Thirdly, there were differences in duration of treatment and flow rate of HFNO in the included trials which may affect the outcomes. For example, HFNO is applied for 15 hours in Futier's study but 48 hours in Parke's.27,28 Different flow rates produce different PEEP, which may have different effects on preventing atelectasis related to hospital LOS.[55] Finally, we found that HFNO reduced the hospital LOS, but failed to change the reintubation rate and the incidence of PPCs which had a downward trend. The reason may be that there are many factors affecting the postoperative hospital LOS, such as the patient's risk status, local and individual clinical practice in addition to PPC,[56] while PPC incidence and intubation rate are not only depend on HFNO but also on patient-related risk factors, type of surgery, and anesthetic technique which requires more detailed data for further analysis.

Conclusion

The meta-analysis of available RCTs suggests prophylactic or therapeutic HFNO consistently shows positive effects on shorter hospital LOS in postoperative patients. The evidence of benefit is promising, but additional well-designed, adequately powered RCTs that meet the following criteria are required: explicitly define criteria for inclusion of postoperative populations, fully evaluate the net clinical benefits on different causes of respiratory failure in different types of surgical patients and mortality associated with HFNO, and comparing the different noninvasive respiratory supports.

Authors' Note

Drs Zhonghua Lu and Fengmei Guo had full access to all the data in the study and take responsibility for its integrity and the accuracy of the data analysis. Drs. Zhonghua Lu, Shanshan Meng, and Fengmei Guo performed the systematic review, study selection, statistical analysis, and elaboration of the article for publication. Drs. Wei Chang, Jianfeng Xie, and Ming Xue contributed to the data extraction and quality assessment. All the authors participated in the article writing and figure elaboration. For information regarding this article, e-mail: luzhonghua077@126.com

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Supplemental Material

Supplemental material for this article is available online.

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