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High-flow nasal cannula therapy versus conventional oxygen therapy for adult patients after cardiac surgery: A systemic review and meta-analysis

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ABSTRACT

Background: Oxygen therapy constitutes a crucial element of post-cardiac operative care. The study assessed the effectiveness of high-flow nasal cannula (HFNC) in comparison to conventional oxygen therapy (COT).
Objectives: The aim of the study was to assess the effectiveness of HFNC in comparison to COT for adult patients following cardiac surgery.
Methods: We conducted a comprehensive search of Embase, PubMed, Scopus, Cochrane Library, and Web of Science databases from inception until April 18, 2023, to identify randomized controlled trials (RCTs) and crossover studies that compared the efficacy of HFNC with COT in adult patients following cardiac surgery.
Results: The meta-analysis included nine studies, consisting of eight RCTs and one crossover study. Compared with COT, HFNC could reduce the need for escalation of respiratory support (RR 0.67, 95% CI: 0.48 to 0.93, $P = 0.02$), decrease arterial partial pressure of carbon dioxide ($PaCO_2$) levels (MD -3.14, 95% CI: -4.90 to -1.39, $P<0.001$), and increase forced expiratory volume in 1 second (FEV_1) levels (MD 0.08, 95% CI: 0.02 to 0.15, $P = 0.02$). There was no significant difference between the HFNC and COT groups in terms of mortality, intubation rate, respiratory rate, heart rate, intensive care unit and hospital length of stay, arterial partial pressure of oxygen (PaO_2), forced vital capacity, and complications of atrial fibrillation and delirium.
Conclusion: Compared with COT, HFNC could decrease the need for escalation of respiratory support, lower $PaCO_2$ levels, and elevate FEV_1 levels in patients following cardiac surgery.

Introduction

Impairment of respiratory function is a significant barrier for patients following cardiac surgery, leading to elevated morbidity and mortality rates, increased health care costs, prolonged hospital stays, and other adverse clinical outcomes.[1-3] This respiratory dyfunction is caused by various factors, such as alveolar edema, elevated pulmonary vascular pressure, alveolar collapse, altered chest muscle or wall, increased inflammation, and impaired phrenic nerve function.[3,4] Consequently, patients following cardiac surgery are susceptible to hypoxia and potentially respiratory failure. Therefore, it is imperative to establish appropriate interventions to mitigate the risk of respiratory complications in this patient population.

Patients undergoing cardiac surgery have commonly received conventional oxygen therapy (COT), consisting of nasal prongs oxygen, facemask oxygen, venturi mask oxygen, and similar methods. However, COT delivers oxygen concentration via gas and does not offer adequate respiratory support.[5] Additionally, COT is characterized by an unstable oxygen supply concentration and a lack of heating and humidification functions.[6,7] Conversely, non-invasive ventilation (NIV) can provide positive pressure ventilation for patients, but it is associated with certain limitations, such as poor tolerance, prevention of early mobilization, and gastric distension.[8] The potential incidence of NIV failure in patients following cardiothoracic surgery is as high as 20%.[9] Therefore, it is imperative to explore therapeutic interventions that possess the physiological benefits of NIV and address its limitations to improve the postoperative outcomes of cardiac surgery patients.

High-flow nasal cannula (HFNC) therapy presents a promising and

Abbreviations: COT, conventional oxygen therapy; NIV, non-invasive ventilation;HFNC, High-flow nasal cannula; FIO_2, fraction of inspired oxygen; RCTs, Randomized controlled trials; RoB, risk of bias; RRs, relative risks; MDs, mean differences; SMDs, standardized mean differences; BMI, body mass index; ICU, intensive care unit; LOS, length of stay; $PaCO_2$, arterial partial pressure of carbon dioxide; PaO_2, arterial partial pressure of oxygen; FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity.

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innovative approach to oxygen therapy.[10] HFNC can administer a consistent and humidified gas mixture at a maximum flow rate of 60 L/min via a nasal catheter while regulating the fraction of inspired oxygen (FIO_2) within a range of 21%−100%.[10] Furthermore, HFNC has been shown to generate a positive end-expiratory pressure effect and decrease physiological dead space, ultimately reducing the work of breathing.[7,11,12] Because of its theoretical physiological benefits, good tolerance, and comfort, HFNC is commonly used in cases of acute hypoxic respiratory failure, particularly among post-extubation populations and patients infected with SARS-CoV-2.[5,13-15]

Recent research has focused extensively on the comparative efficacy of HFNC and COT, including in cardiac surgery. Two previous meta-analyses compared the use of HFNC and COT in patients following cardiac surgery.[5,16] However, the number of studies included in both analyses was limited. Only two trials were included in the meta-analysis conducted by Zhu et al. ,[5] while only three were included in the meta-analysis conducted by Wang et al. .[16] The findings of these meta-analyses have some limitations. Since 2020, four new randomized controlled trials (RCTs)[17-20] and one new crossover study have been published.[21] A comprehensive and detailed systematic meta-analysis is required to thoroughly evaluate the effectiveness of HFNC in compared to COT for adult patients following cardiac surgery.

Methods

The current meta-analysis was in accordance with PRISMA statement and was registered on PROSPERO (CRD 42023424671).

Data sources and search strategies

A comprehensive search was conducted across Embase, Scopus, Pubmed, Cochrane Library, and Web of Science databases to identify relevant studies published in English from inception to April 18, 2023. The search strategy is described in Supplementary **Table 1.**

Inclusion and exclusion criteria

The inclusion criteria were as follows: (1) RCTs and crossover studies; (2) Adult patients after cardiac surgery; (3) The treatment group underwent HFNC therapy, whereas the control group underwent COT; (4) At least one of the predefined outcomes was reported: escalation of respiratory support, mortality, intubation rate, respiratory rate, heart rate, intensive care unit (ICU) length of stay (LOS), hospital LOS, arterial blood gas index (arterial partial pressure of carbon dioxide [$PaCO_2$] and arterial partial pressure of oxygen [PaO_2]), pulmonary function measurements (forced expiratory volume in 1 second [FEV_1] and forced vital capacity [FVC]), and complications of atrial fibrillation and delirium. Exclusion criteria were as follows: conference abstracts, letters, case reports, and review articles; non-English literature; non-RCT and crossover design; participants younger than 18 years.

Outcomes

The primary endpoints was escalation of respiratory support rates. Secondary outcome measures included mortality rates, intubation rates, respiratory rate, heart rate, ICU LOS, hospital LOS, arterial blood gas index, FEV_1, FVC, and complications of atrial fibrillation and delirium. The escalation of respiratory support treatment was defined as crossover to HFNC in the COT group, or initiation of noninvasive ventilation or invasive mechanical ventilation in either group.

Study selection

Two researchers independently screened titles and abstracts and excluded duplicates and non-RCT/non-crossover literature. Any potentially relevant literature would undergo a full-text screening. Studies that met the inclusion criteria were obtained by searching the full text. Any disagreements or controversies were resolved by consulting a third researcher.

Data extraction and analysis

A pre-designed data extraction table was used to extract the characteristics of the included studies (author name, publication year, region, sample size), characteristics of participants (age, sex, body mass index [BMI], bypass time), HFNC parameter setting (Flow rate, FIO_2), COT parameter settings (Flow rate, FIO_2), and the outcomes of interest.

Quality assessment

Two researchers independently assessed the risk of bias (RoB) through the Cochrane Risk of Bias tool.[22] If there was any disagreement, an agreement was reached through discussion with the third researcher. The RoB assessment includes several aspects: selection bias, performance bias, detection bias, attrition bias, reporting bias, and other biases.[22] For each domain, RoB was rated as "yes," "no," or "unclear," to indicate a high, low, or uncertain risk of bias, respectively.

Statistical analysis

Review Manager software (Version 5.3, The Cochrane Collaboration, Copenhagen, Denmark) was used for meta-analysis. For binary outcomes, relative risks (RRs) with corresponding 95% CI were calculated. Pooled RRs were excluded from studies with no event in either arm. For continuous variables, mean differences (MDs) or standardized mean differences (SMDs), with corresponding 95% CI were calculated. When required, medians and interquartile ranges were converted to means and standard deviations for the meta-analysis.[23] Pooled MD or SMD with 95% CI were estimated using the inverse variance method. We visually inspected the potential publication bias with a funnel plot if ten or more studies existed for a given outcome.[24] We used DerSimonian- Laird random effects models for pooling outcomes. Significant heterogeneity was defined as having a chi^2 P value<0.1 or an $I^2>50\%$.[25]

Sensitivity analysis

We performed a sensitivity analysis of the analyzed outcomes to test the robustness of the results by excluding one study with a randomized crossover design.[21]

Trial sequential analysis

A trial sequential analysis (TSA)[26] was conducted using a random effects model for escalation of respiratory support, mortality, and intubation outcomes. For TSA, a statistical significance level of 5%, power of 80%, and the O'Brien–Fleming-spending function were used. For dichotomous data, the required information size was calculated based on a relative risk reduction of 20%. TSA was performed using Trial Sequential Analysis v.0.9.5.10 beta (Copenhagen Trial Unit, centre for Clinical Intervention Research, Rigshospitalet, Copenhagen, Denmark; www.ctu.dk/tsa).

Ethical issues

This literature-based meta-analysis did not involve direct contact with patients. Therefore, ethics committee approval was not required for our study.

Results

The initial search found 2036 studies. After removing duplicates, 1769 references were identified. We further reviewed the full text of 53

references and finally included 9 studies in our meta-analysis (eight RCTs[17-20,27-30] and one crossover study[21]). The screening process and results are shown in Fig. 1.

Characteristics of the included studies

We included 1121 participants in our meta-analysis. Of the nine studies included, 73.1% (820) were male. Seven studies[17,18,20,21,27,29,30] are single-central trials. One of the nine randomized trials adopted a crossover design.[21] Table 1 outlines the included study characteristics and baseline patient characteristics.

Quality assessment

The results of the risk of bias evaluation of the included studies are shown in Fig. 2. All included studies exhibited high levels of performance bias due to the inability of any study to blind participants and staff. One study[29] did not clearly describe allocation concealment. Two studies[17,18] have clearly described the information on blinding of outcome assessment. In addition, the nine studies demonstrated the method of random sequence generation and lacked any bias in attribution and reporting.

Escalation of respiratory support

Five studies[18,20,27-29] reported data on treatment escalation. HFNC therapy may reduce the need for treatment escalation compared to COT (RR 0.67, 95% CI: 0.48 to 0.93, $z = 2.39$, $P = 0.02$) (Fig. 3A).

Mortality

Four studies[18,19,27,29] provided mortality data. Compared with COT, HFNC therapy showed no difference (RR 0.48, 95% CI: 0.06 to 3.69, $z = 0.70$, $P = 0.48$) (Fig. 3B).

Endotracheal intubation rate

The pooled incubation rate estimate was derived from five studies.[18-20,28,29] No difference in intubation rates was found between HFNC therapy and COT (RR 0.93, 95% CI: 0.24 to 3.63, $z = 0.10$, $P = 0.92$) (Fig. 3C).

ICU length of stay and hospital length of stay

Six studies[18-20,27-29] measured the ICU length of stay. HFNC had no effect on ICU LOS (SMD 0.03, 95% CI: −0.14 to 0.20, $z = 0.32$, $P = 0.75$) (Fig. 4A). Data on hospital LOS were available from five studies.[17,20,27,29,30] Similarly, no difference in hospital LOS was found between HFNC therapy and COT (MD −0.57, 95% CI: −1.72 to 0.58, $z = 0.97$, $P = 0.33$) (Fig. 4B).

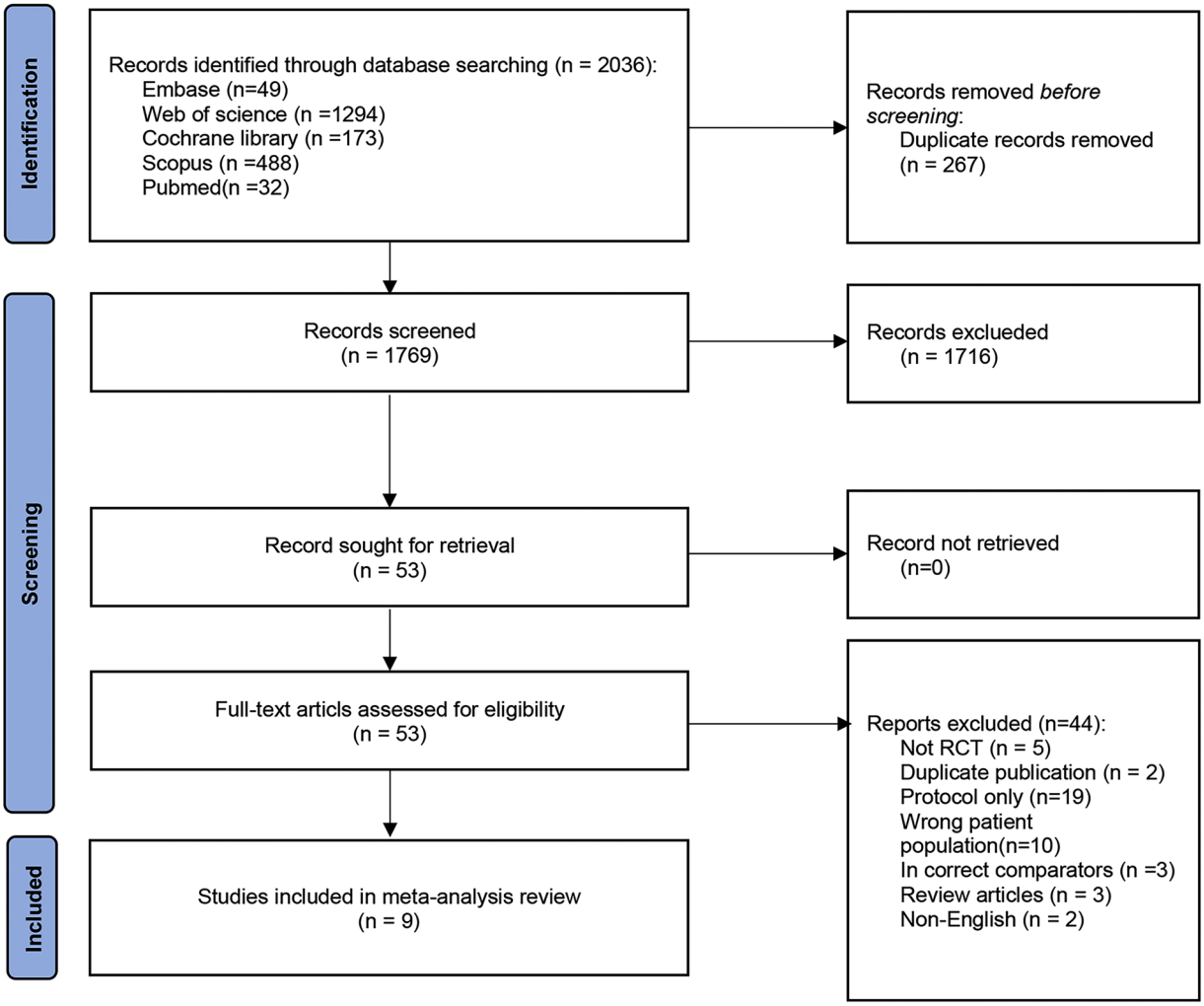

Fig. 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses flowchart of the study selection process.

Table 1
Details of the included studies.

Study	Country	Study design	Sample size	Male	Age, y	Surgery type	Bypass time, min	BMI, kg/m^2	FIO_2	Duration for treament	HFNC		COT
											Flow rate, L/min	Delivery method	Flow rate, L/min
Parke 201,3[27]	New Zealand	Single-center open-label RCT	340	258	57.7 ± 49.4	Elective cardiac surgery(CABG, valve surgery, both, or other)	110±53	28.8 ± 5.4	Maintain a SpO_2 of 93%.	HFNC:59 ±30.8 h; COT:65±41.6 h	45	Simple facemask or nasal prongs	2–4
Corley 201,5[28]	Australia	RCT	155	148	64.0 ± 11.3	Elective cardiac surgery(CABG, valve surgery, both, or other)	99.5 ± 48.7	35.5 ± 4.8	Maintain a $SpO_2 \geq 95\%$	8h	35–50	Nasal cannulae or simple face mask	2–4 via nasal cannulae or 6 L/min via simple face mask
Zochios 201,8[30]	UK	Single-center RCT	94	58	68.2 ± 10.2	Elective cardiac surgery (CABG, valve surgery or both)	NA	31.1 ± 6.1	Maintain a $SpO_2 \geq$ 95% (93% for those at risk of hypercapnic respiratory failure,	24h	20–50	Nasal prongs or a soft facemask	NA
Tatsuishi 202,0[17]	Japan	Prospective single-blinded RCT	148	113	69.0 ± 8.6	Off pump coronary artery bypass graft surgery	NA	NA	21–35%	≤24h	45–60	Standard oxygen mask	3–12
Vourc'h 202,0[18]	France	Single-center prospective, and open-label RCT	90	77	66.7 ± 9.8	Coronary artery bypass surgery	91±26.3	29.2 ± 4.2	Maintain a SpO_2 of 100%	48h	45	Standard high-flow face mask	15
Burra 202,1[19]	India	prospective RCT	60	43	51.6 ± 14.7	Elective cardiac surgery	NA	22.1 ± 4.7	NA	4h	60	Nasal cannula oxygen	4
Theologou 202,1[20]	Greece	Single-center prospective, unblinded RCT	99	67	67.1 ± 9.1	Elective or urgent cardiac surgery.	129.43 ±54.1	29.3 ± 4.9	HFNC group 1:60%; HFNC group2: 60%	≤48h	HFNC gourp1:60 L/min;HFNC group2: 40 L/min	Venturi mask	15
Shiho 202,2[21]	Japan	Single-center RCT	35	20	69 ±10.3	Elective cardiac surgery	NA	22.0 ± 4.9	NA	1h	40	Venturi mask	40
Sahin 201,8[29]	Turkey	Single-center, prospective RCT	100	36	61.7 ± 7.6	CABG	91.0 ± 12.6	32.4 ± 1.1	Initial FIO_2 was 50% to maintain $SaO_2 > 93\%$	48h	25–40	Simple face mask	2–4

BMI, body mass index; RCT, randomized controlled trial; CABG: coronary artery bypass grafting; FIO_2, fraction of inspired oxygen; Spo2, blood oxygen saturation; HFNC, high-flow nasal cannula; NA, not applicable.

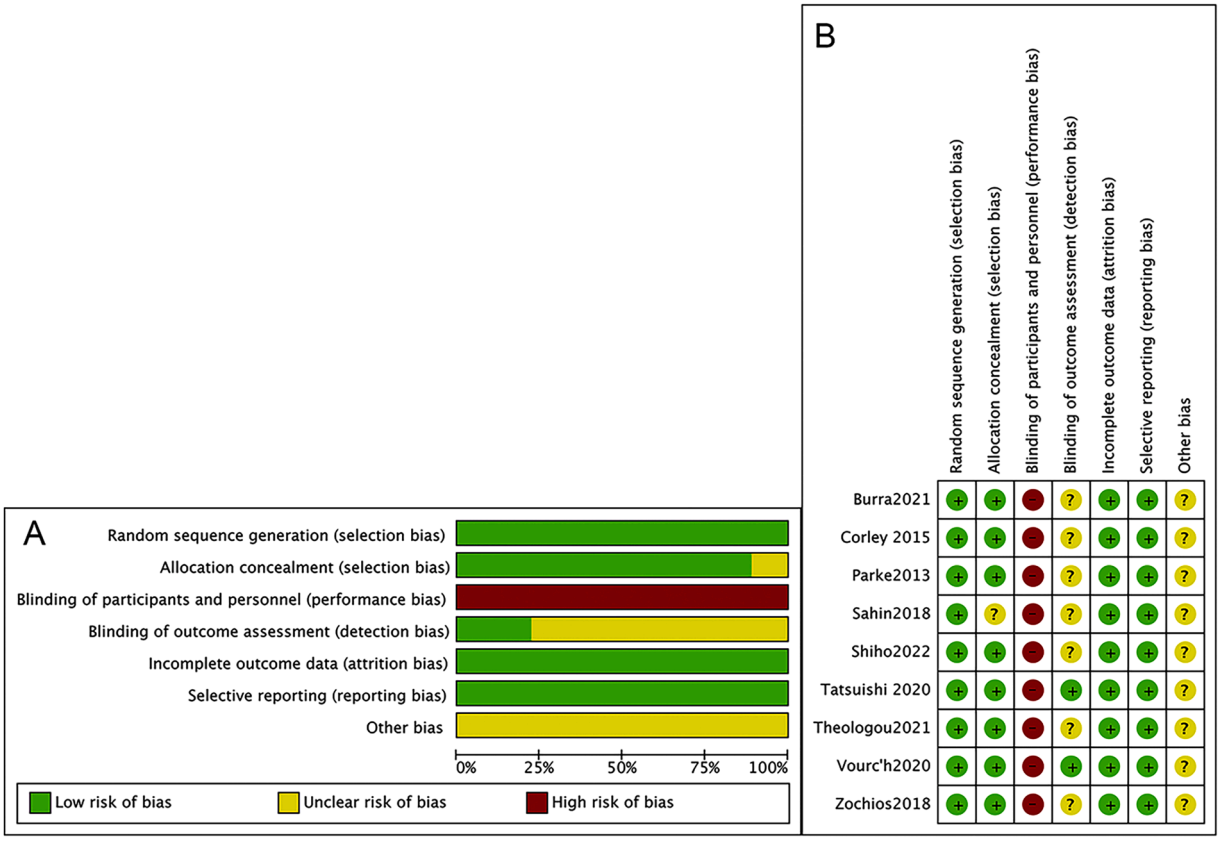

Fig. 2. Risk of bias. Risk of bias graph: judgements about each risk of bias item presented as percentages across all included studies (A); risk of bias summary: judgements about each risk of bias item for each included study (B). Red, high risk of bias; Green, low risk of bias; yellow, unclear risk of bias.

Respiratory rate and heart rate

Respiratory rate data were available from three studies.[18,21,29] No difference was found between HFNC therapy and COT (MD −1.11, 95% CI: −2.57 to 0.36, $z = 1.48$, $P = 0.14$) (Fig. 5A).

Heart rate data were found from two studies.[18,29] Compared to COT, HFNC therapy had no effect on heart rate (MD 0.27, 95% CI: −1.29 to 1.83, $z = 0.34$, $P = 0.73$) (Fig. 5B).

Arterial blood gas index PaO_2 and $PaCO_2$

Three studies[19,21,29] reported data on PaO_2, and three studies[19,21,29] reported data on $PaCO_2$. $PaCO_2$ in the HFNC group was significantly lower than in the COT group (MD −3.14, 95% CI: −4.90 to −1.39, $z = 3.51$, $P<0.001$) (Fig. 6A). However, no difference in PaO_2 level was observed (MD 83.73, 95% CI: −5.24 to 172.70, $z = 1.84$, $P = 0.07$) (Fig. 6B).

Pulmonary function measurements

Data on FEV_1 and FVC were available from three studies.[27,29,30] Two studies explicitly specified the timing of pulmonary function testing, which was completed at discharge[27] and on the fifth or sixth day after surgery.[29] In contrast, one study did not provide specific information on the completion time of lung function testing, but only stated that it was conducted during the postoperative follow-up period.[30]

HFNC therapy may increase FEV_1 level compared to COT (MD 0.08, 95% CI: 0.02 to 0.15, $z = 2.43$, $P = 0.02$) (Fig. 7A). There was no difference in FVC level between HFNC therapy and COT (MD 0.28, 95% CI: −0.18 to 0.73, $z = 1.20$, $P = 0.23$) (Fig. 7B).

Atrial fibrillation and delirium complications

Three studies[20,29,30] reported data on atrial fibrillation complications. No difference was found in atrial fibrillation complications between HFNC therapy and COT (RR 0.73, 95% CI: 0.28 to 1.91, $z = 0.65$, $P = 0.52$) (Fig. 8A).

Delirium complication data were available from two studies.[20,30] Similarly, HFNC therapy did not reduce delirium occurrence compared to COT (Fig. 8B).

Sensitivity analysis and publication bias

The PaO_2 and respiratory rate results of the analyzed outcomes were unaffected by sensitivity analyses that excluded a crossover design study[21] (Supplementary Fig. 1–2). However, there was no difference in the $PaCO_2$ outcome between HFNC therapy and COT after excluding a crossover design study (Supplementary Fig. 3). Meanwhile, no funnel plot test was performed, as no study outcome included more than 10 studies.

Trial sequence analysis

The cumulative z-curve of escalation of respiratory support surpassed the traditional boundary; however, it did not meet the RIS, and the boundaries for benefit, harm, or futility were not crossed(Supplement Fig. 4). The TSA results for mortality and intubation showed that overall effect outcomes were inconclusive, as the cumulative z-curve did not meet the RIS, and the boundaries for benefit, harm, or futility were not crossed (Supplement Fig. 5-6). This finding suggests the necessity for additional research to validate the benefits of HFNC over COT with increased confidence.

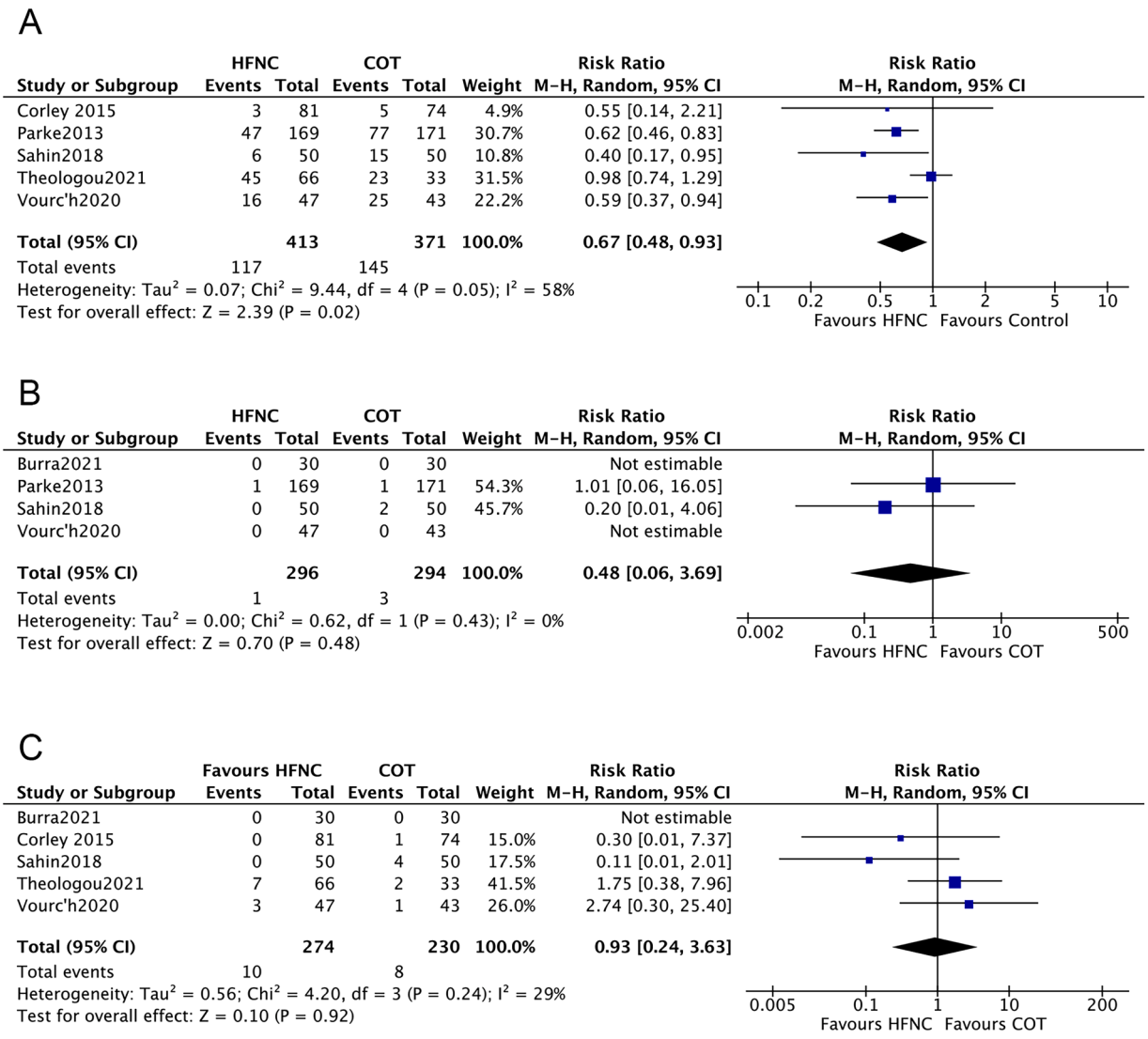

Fig. 3. Forest plot of escalation of respiratory support(A), mortality(B), and intubation(C). HFNC, high-flow nasal cannula oxygen; COT, conventional oxygen therapy; M-H, Mantel-Haenszel; CI, confidence interval.

Discussion

Our meta-analysis demonstrated that HFNC therapy, compared to COT, could potentially reduce the need for treatment escalation, decrease $PaCO_2$ levels, and increase FEV_1 levels in patients following cardiac surgery. These findings support the notion that HFNC could be a viable alternative to COT in the treatment of post-cardiac surgery patients.

According to our study, HFNC may reduce the need for treatment escalation. This finding supports a previous meta-analysis[31] that included two studies. The clinical significance of the reduced requirement for treatment escalation is noteworthy, particularly in light of the potential for increased morbidity, mortality, and length of stay associated with increase use of invasive ventilation and NIV.[9,31,32]

HFNC did not demonstrate superiority over COT in improving mortality and length of stay. This finding can be attributed to factors beyond respiratory function that influence mortality and length of stay. Consequently, further research is needed to identify the population most likely to benefit from HFNC.

Two studies[9,16] found no significant differences in ICU LOS and intubation rates. Our analysis supports and enhances these results by incorporating additional RCTs. Unlike previous meta-analyses, our study incorporated recently reported outcomes, such as atrial blood gas indices, pulmonary function measurements, complications of atrial fibrillation and delirium, respiratory rate, and heart rate, providing a more comprehensive evaluation.

This study found that HFNC use was associated with a decrease in $PaCO_2$ levels and an increase in FEV_1 levels compared to COT. The high gas flows delivered by HFNC may potentially increase the mean airway pressure and facilitate the elimination of dead space, as suggested by several physiological studies.[33,34]

Moreover, observational studies[35,36] have demonstrated the efficacy of HFNC therapy in ameliorating hypercapnia. Several meta-analyses[24,37] have suggested that HFNC may be non-inferior to NIV in the management hypercapnic respiratory failure. Given the benefits of enhanced patient comfort and reduced complications, HFNC may represent a viable alternative to NIV.[37] However, the use of HFNC in patients with hypercapnic respiratory failure following cardiac surgery has not been extensively explored in recent investigations. Our findings may therefore serve as a preliminary basis for further research into the potential application of HFNC in patients after cardiac surgery with hypercapnia. Further studies evaluating the effects of HFNC on $PaCO_2$ with more participants are needed to provide robust evidence because most trials had a small sample size.

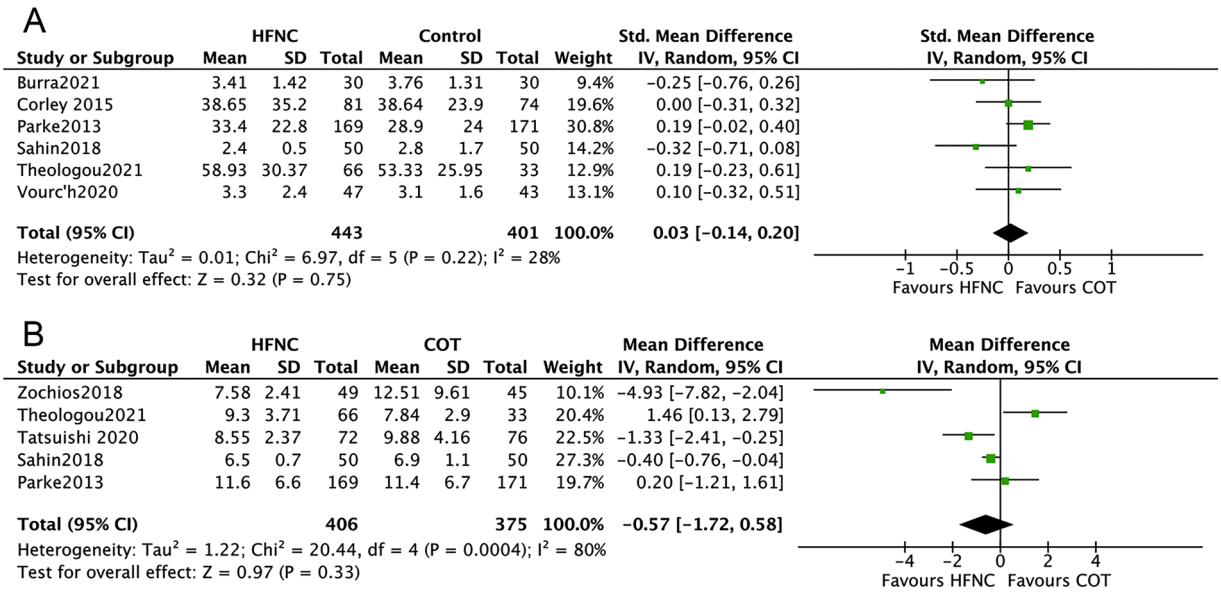

Fig. 4. Forest plot of ICU length of stay (A) and hospital length of stay (B). HFNC, high-flow nasal cannula oxygen; COT, conventional oxygen therapy; M-H, Mantel-Haenszel; CI, confidence interval.

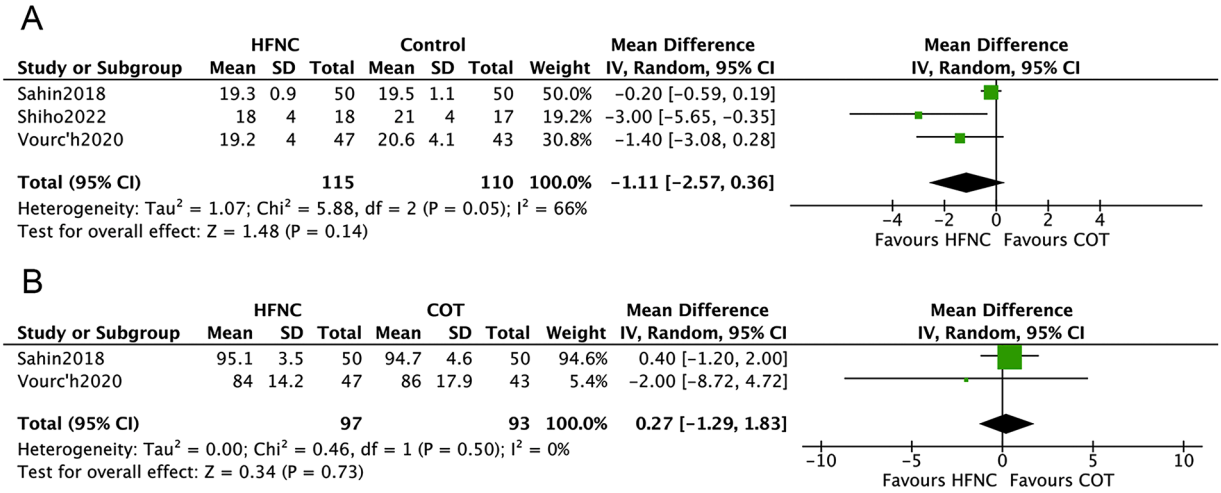

Fig. 5. Forest plot of respiratory rate (A) and heart rate (B). HFNC, high-flow nasal cannula oxygen; COT, conventional oxygen therapy; M-H, Mantel-Haenszel; CI, confidence interval.

The potential for HFNC to increase postoperative FEV_1 levels, a phenomenon not previously observed in the existing literature, warrants further exploration. The decline in pulmonary function following cardiac surgery may be related to dyspnea, impaired coughing ability, and adverse clinical outcomes.[1,2] The current meta-analysis included only three studies that reported the effects of HFNC compared to COT on pulmonary function parameters. Of the three studies, only two specifically specified the timing of pulmonary function testing, which was completed at discharge[27] and on the fifth or sixth day after surgery.[29] In addition, given that the duration of HFNC treatment only last 24 or 48 h, the effect of HFNC on pulmonary function measurements, especially the long-term effect, needs to be explored in the future.

The findings from our meta-analysis are highly relevant for clinical practice, as they provide evidence that patients receiving HFNC therapy after cardiac surgery have a significantly lower risk of treatment escalation and improved respiratory function as measured by FEV_1. Given the significant benefits of HFNC in this study, clinicians should carefully consider the potential benefits of HFNC over COT when making treatment recommendations and determining the optimal postoperative oxygen therapy strategies for cardiac surgery patients.

Limitations

Our study has several limitations. First, the setting of the HFNC flow rate and the application of COT were inconsistent among the included studies, which may account for the heterogeneity. Second, we cannot do the funnel figures to detect publication bias because the number of included studies was less than 10. Third, almost all included studies (7/9) were conducted in a single center, which may have led to bias. Fourth, in spite of the more and more studies as the evidence, according to the TSA results, further well-designed RCTs with large population sizes are still needed to assess the effects of HFNC, especially, escalation of respiratory support, mortality and intubation, on patients following cardiac surgery.

Conclusion

HFNC therapy may reduce the need for treatment escalation and

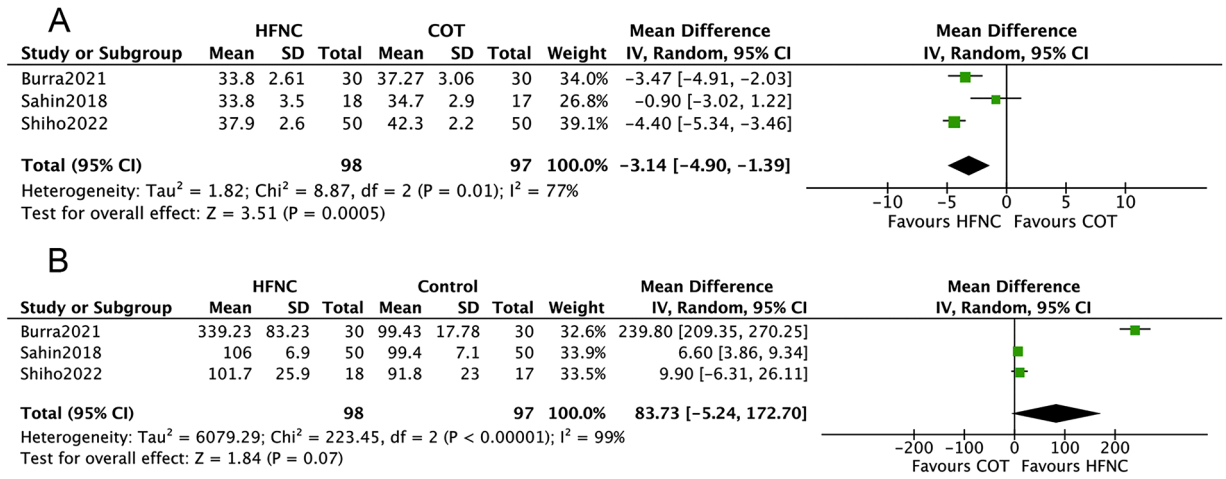

Fig. 6. Forest of arterial blood gas index. Forest plot of $PaCO_2$ (A); Forest plot of PaO_2 (B). HFNC, high-flow nasal cannula oxygen; COT, conventional oxygen therapy; M-H, Mantel-Haenszel; CI, confidence interval.

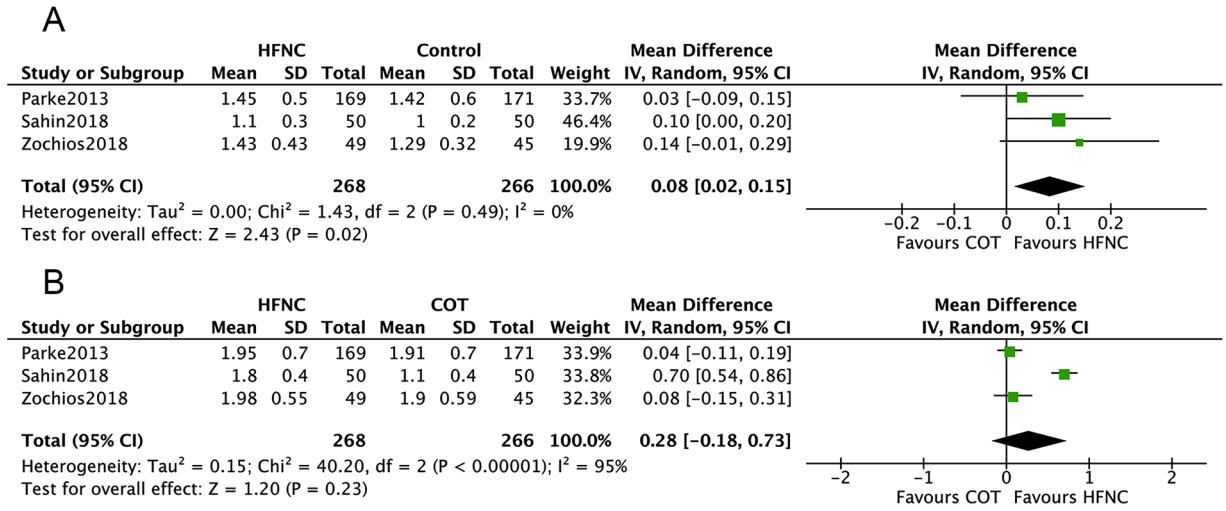

Fig. 7. Forest of pulmonary function measurements.Forest plot of FEV_1 (A); Forest plot of FVC (B). HFNC, high-flow nasal cannula oxygen; COT, conventional oxygen therapy; M-H, Mantel-Haenszel; CI, confidence interval.

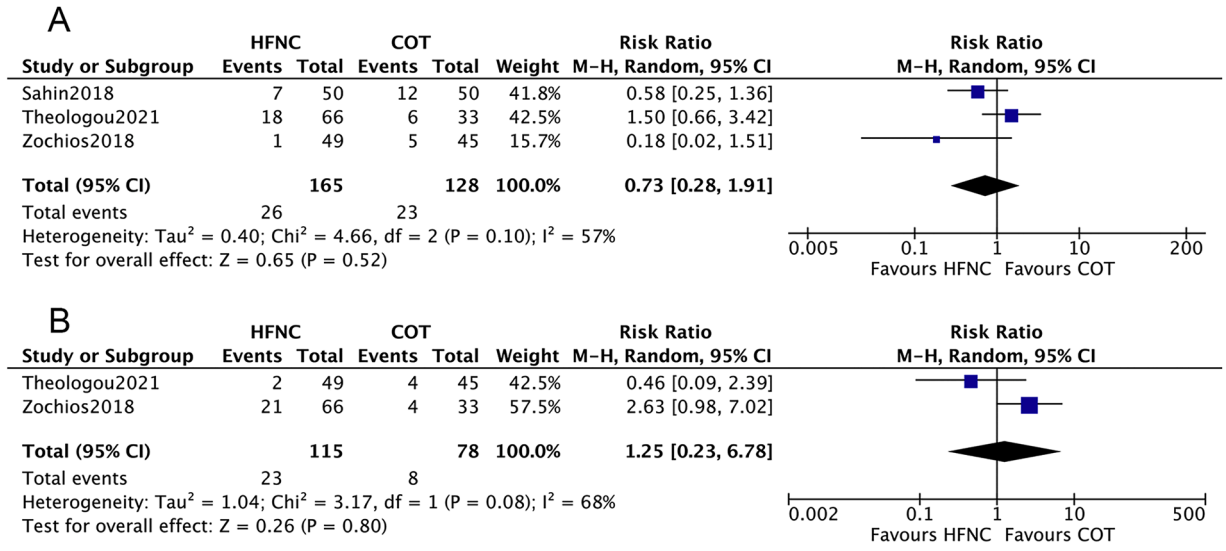

Fig. 8. Forest of atrial fibrillation (A) and delirium complications (B). HFNC, high-flow nasal cannula oxygen; COT, conventional oxygen therapy; M-H, Mantel-Haenszel; CI, confidence interval.

lower $PaCO_2$ levels while simultaneously increasing FEV_1 levels in patients following cardiac surgery, compared to COT. Therefore, HFNC may represent a viable alternative to COT in treating patients following cardiac surgery. However, the present findings require further validation through large-scale, multicenter studies.

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CRediT authorship contribution statement

Chuantao Liu: Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Software, Methodology, Investigation, Formal analysis, Data curation. **Qihong Lin:** Software, Methodology, Formal analysis, Data curation. **Dongyu Li:** Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Software, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.hrtlng.2024.03.008.

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