Original Article

High-Flow Nasal Cannula vs. Incentive Spirometer after Cardiac Surgery: A Randomized Controlled Trial

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Background: Respiratory care after cardiac surgery is a challenging area of medical treatment. High-flow nasal oxygen cannula (HFNC) may be used for reducing the reintubation rate.

Objective: The present study aimed to compare the use of HFNC with that of an incentive spirometer (IS) with respect to the reintubation rates in patients after cardiac surgery.

Materials and Methods: The authors conducted a prospective randomized controlled trial of 67 cardiac surgery patients. The HFNC group received the HFNC immediately after extubation performed within 24 hours, and the IS group received the IS with breathing exercises. Reintubation, length of intensive care unit, length of hospital stay, ratio of arterial partial pressure of oxygen to fraction of inspired oxygen (PaO_2/FiO_2), partial pressure of carbon dioxide ($PaCO_2$), and peak expiratory flow rate (PEFR) were analyzed and compared.

Results: The reintubation rate was higher in the HFNC group, but the difference was not statistically significant (p=0.054). Hypoxia was the most common cause of intervention failure at 29.4% and 24.2% in the HFNC and IS groups, respectively. Four (11.8%) reintubated patients in the HFNC group later progressed to hospital-acquired pneumonia, which resulted in longer hospital stays (p=0.010). The PaO_2/FiO_2 ratio and PEFR decreased by 33.5% and 62.5%, respectively, on postoperative day 1 and improved the following day. The $PaCO_2$ was within the normal limits in both groups.

Conclusion: Compared to IS, prophylactic HFNC 24 hours after cardiac surgery increased the reintubation rate, but not significantly. The decision to administer prophylactic HFNC support after extubation in cardiac surgery patients should be contemplated on an individual basis.

Trial registration: This trial is registered at clinicaltrials.in.th, Thai Clinical Trials Registry, TCTR20180201001.

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Reintubation is frequently required within 24 hours in up to 3.82% of patients who underwent cardiac surgery[1]. After cardiac surgery, most patients experience atelectasis, a common pulmonary complication[2] associated with pneumonia and remains the most common cause of hospital-acquired infection (up to 6% of cases)[3]. During this period, respiratory care should be optimized. Appropriate chest physiotherapy can promote full inspiration and expiration, thereby reducing the incidence of postoperative pulmonary complications.

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After cardiac surgery, when patients are extubated and oxygen supplementation is tapered off, an incentive spirometer (IS) with breathing exercises is routinely used in most institutions to enhance recovery. The use of a high-flow nasal oxygen cannula (HFNC) is an alternative method for delivering inspired oxygen flow at up to a rate of 60 L/minute, and it provides positive end-expiratory pressure and the desired temperature and humidity[4], it can be inserted easily and eases patient respiration and promotes better rehabilitation. In low-risk non-surgical patients, using an HFNC after extubation may reduce the rate of reintubation compared to that noted with conventional oxygen therapy[5]. However, in cardiac surgery patients whose normal chest physiology may be impaired from sternotomy, the advantages of HFNC are still not clear[6]. The present study aimed to compare the rate of reintubation between patients who received prophylactic HFNC within 24 hours and patients who received IS with breathing exercises after extubation following cardiac surgery.

Materials and Methods

The authors conducted a prospective randomized control trial at the Cardiovascular Thoracic Surgery Unit, Rajavithi Hospital between March 1, 2018 and November 30, 2018. The present study was conducted according to the guidelines of the Declaration of Helsinki, and written informed consents were obtained from all patients; ethical approval was obtained from the authors' Institutional Ethics Committee (Rajavithi EC 202/2560), and registered in the Thai Clinical Trials Registry (ID: TCTR20180201001).

Patients

Patients aged ≥18 years undergoing on-pump cardiopulmonary bypass cardiac surgery with median sternotomy were included. The exclusion criteria were emergency surgery, active pulmonary disease, abnormal chest imaging, room air oxygen saturation (O_2Sat) <95%, ratio of arterial partial pressure of oxygen to fraction of inspired oxygen (PaO_2/FiO_2) <300 mmHg, prolonged intubation >48 hours, reoperation due to any cause, self-extubation, and refusal to participate.

Study intervention

All patients were promoted for early extubation if their hemodynamic status were stable, but if the operation finished at nighttime (after 8 p.m.), extubation was performed in the morning instead. Pain control was managed by administration of low dose of opioids to maintain a pain score ≤4. The extubation criteria included all of the following: 1) stable hemodynamic status, 2) respiratory rate <25 breaths per minute, 3) no respiratory accessory muscle use, 4) PaO_2 ≥70 mmHg or SaO_2 ≥92%, or PaO_2/FiO_2 ≥350 mmHg, 5) full consciousness, and 6) passing a spontaneous breathing test.

In the HFNC group, patients received HFNC (Optiflow, Fisher & Paykel Healthcare, Auckland, New Zealand) for 24 hours, starting immediately after extubation. An FiO_2 between 0.21 to 1.0 was set by adjusting the airflow from 20 to 60 L/minute to achieve the target O_2Sat ≥92% on plethysmography.

In the IS group, patients were advised to perform deep breathing exercises using an IS (Triflo II Inspiratory Exerciser, Teleflex Inc., Temecula, CA, USA) with a slow sustained maximal inspiration of at least 600 ml/second. Patients were advised to perform this exercise 5 to 10 times per waking hour. Oxygen supplementation with a simple oxygen cannula or mask with a bag was considered for maintaining target O_2Sat ≥92% on plethysmography.

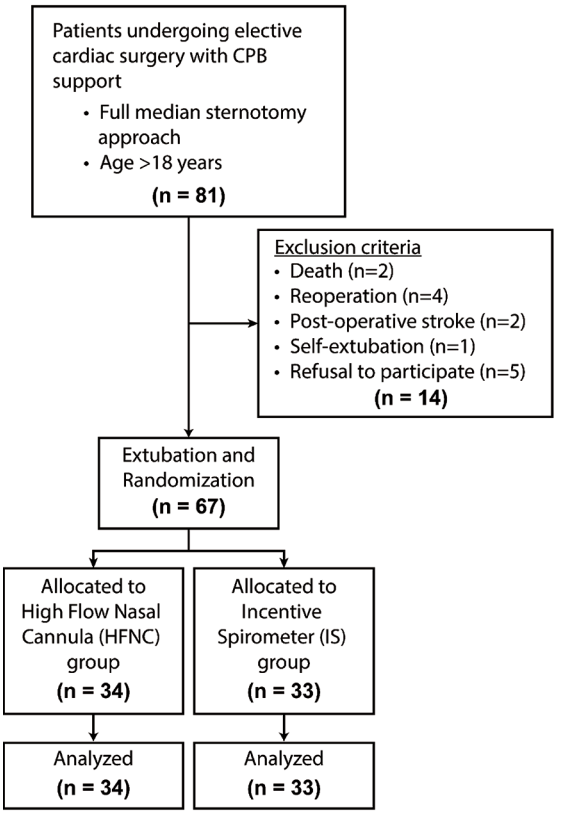

Figure 1. Flowchart of the study protocol.
CPB=cardiopulmonary bypass

Arterial blood gas analysis data were collected using an arterial catheter preoperatively to post-operative day 3 to measure the PaO_2, partial pressure of carbon dioxide ($PaCO_2$), and PaO_2/FiO_2. The peak expiratory flow rate (PEFR) was measured using a peak flow meter from postoperative day 1 to postoperative day 5 as a measure of pulmonary function.

Randomization

Patients were randomly assigned to either the HFNC or IS treatment group using computer-assisted randomization, regardless of the entry criteria. Allocation was concealed in a sealed and opaque envelope that was sequentially numbered by an uninvolved attendant and assigned to the patient after extubation by the attending nurse (Figure 1).

Intervention failure and reintubation

Intervention failure was defined when at least one of the following criteria were met within 24 hours: 1) respiratory rate ≥25 breaths per minute or signs of

respiratory accessory muscle use, 2) O_2Sat <92% or PaO_2<60 mmHg despite a maximum flow rate of 60 L/minute via the HFNC or of 10 L/minute via the oxygen mask with a bag in the IS group, 3) $PaCO_2$ ≥50 mmHg, 4) unstable hemodynamic status, or 5) worsening consciousness.

A full-face cover mask using non-invasive ventilation (NIV) with positive pressure support was applied immediately if the patient met any of the aforementioned criteria. Reintubation was considered when NIV did not improve the patient's condition, which was re-evaluated every hour.

Outcomes

The primary outcome was reintubation. The secondary outcomes were length of intensive care unit (ICU) stay, length of hospital stay, PaO_2/FiO_2 ratio, $PaCO_2$, and PEFR.

Statistical analysis

Based on a high-flow nasal oxygen cannulation rate of 10% and a standard therapy rate of 30% in the ICU[7], it was estimated that 62 patients were needed in each group to provide 80% power and a two-sided significance level of 0.05. The continuous variables were examined for normal distribution using the Kolmogorov-Smirnov test and expressed as mean ± standard deviation when normally distributed or median (interquartile range [IQR]) when non-normally distributed. The categorical variables were presented as absolute number and percentage. Comparisons between the two groups were performed using the Student t-test or Mann-Whitney U test for the continuous variables, as appropriate, and a Fisher's exact test for the categorical variables. A p-value of 0.05 or less indicated statistical significance. Statistical analyses were performed using the R Statistical package version 3.6.1 (R Foundation for Statistical Computing, Vienna, Austria).

Results

Of the 81 patients enrolled in the present study, 14 patients were excluded. A total of 67 were included and randomized. The patient baseline characteristics were almost identical in the two groups (Table 1). However, the median age was significantly higher in the HFNC group [64 years (IQR 56 to 69) vs. 60 years (IQR 50 to 64) in the IS group, p=0.045], and more patients in the HFNC group underwent combined procedures (eight patients (23.5%) vs. 0 patients (0%) in the IS group, p=0.005). The combined procedures in the HFNC group included valve + aortic surgery in four patients, coronary artery bypass graft + aortic surgery in two patients, and valve + closure of atrial septal defect in two patients. Most of these patients had the New York Heart Class II and III disease, and the median left ventricular ejection fraction was 60%; therefore, they were not candidates for prolonged intubation or successful postoperative rehabilitation. The preoperative PEFR, PaO_2, and PaO_2/FiO_2 ratio were similar between the two groups and within the normal limits. The aortic cross clamping time was slightly higher in the HFNC group, but the difference was not significantly different (99±47 minutes vs. 80±28 minutes, p=0.054). The total intubation time (hours) was similar in both groups [median 15.3 hours (IQR 12.7 to 18.9) vs. median 13.4 (IQR 9.1 to 17.2), p=0.156].

Primary outcome

The rate of intervention failure within 24 hours was similar in both groups (HFNC 29.4% vs IS 24.2%, p=0.784) (Table 2). The causes of intervention failure in the HFNC group included hypoxia with secretion obstruction in four (40%) patients, signs of respiratory accessory muscle use in two (20%) patients, unstable hemodynamic status in two (20%) patients, hypercapnia in one (10%) patient, and tension pneumothorax in one (10%) patient. Hypoxia was the most common cause of intervention failure in the IS group [five (62.5%) patients], and three (37.5%) patients showed signs of respiratory accessory muscle use. The rate of reintubation was higher in the HFNC group, but the difference was not statistical significant (20.6% vs 3%, p=0.054). Four (11.8%) reintubated patients in the HFNC group later progressed to hospital-acquired pneumonia, which was not observed in the IS group. In the HFNC group, the leading cause of reintubation was secretion obstruction and hypoxia in four (57.1%) patients, unstable hemodynamic status in two (28.6%) patients, and tension pneumothorax in one (14.3%) patient; whereas, in the IS group only one patient was reintubated due to severe hypoxia. The time to reintubation was not different between the two groups [median 40.8 hours (IQR 8.5 to 45) in the HFNC group vs. median 57.8 hours (IQR 57.8) in the IS group, p=0.275].

Secondary outcomes

The hospital stay was longer in the HFNC group [median 9 days (IQR 7 to 12) vs. median 8 days (IQR 6 to 9) in the IS group, p=0.010] (Table 2). The length of ICU stay was similar in both groups [median 3 days (IQR 2 to 5) in the HFNC group and

Table 1. Patient characteristics

Variable	HFNC (n=34); n (%)	IS (n=33); n (%)	p-value
Age (years); median (IQR)	64 (56 to 69)	60 (53 to 64)	0.045*
Male	22 (64.7)	17 (51.5)	0.456
Height (cm); median (IQR)	161 (154 to 168)	158 (158 to 166)	0.498
Weight (kg); mean±SD	63.7±14.7	61.9±10.5	0.547
Body surface area (m^2); mean±SD	1.7±0.2	1.7±0.2	0.751
Body mass index (kg/m^2); median (IQR)	25 (20 to 28)	25 (21 to 27)	0.985
Underlying condition			
Smoker	7 (20.6)	8 (24.2)	0.776
Diabetes	9 (26.5)	10 (30.3)	0.791
Hypertension	22 (64.7)	14 (42.4)	0.088
Dyslipidemia	16 (47.1)	18 (54.5)	0.809
Atrial fibrillation	3 (8.8)	2 (6.1)	1.000
ESRD with HD	1 (2.9)	2 (6.1)	0.614
CKD without HD	5 (14.7)	4 (12.1)	1.000
COPD	2 (5.9)	2 (6.1)	1.000
NYHC			
1	3 (8.8)	3 (9.1)	1.000
2	23 (67.6)	21 (63.6)	1.000
3	7 (20.6)	8 (24.2)	0.800
4	1 (2.9)	1 (3.0)	1.000
Operation			
Coronary surgery	13 (38.2)	16 (48.5)	0.464
Valve surgery	12 (35.3)	15 (45.5)	0.322
Aortic surgery	1 (2.9)	1 (3.0)	1.000
Congenital surgery	0 (0.0)	1 (3.0)	0.493
Combined procedure	8 (23.5)	0 (0.0)	0.005*
Previous cardiac surgery	3 (8.8)	5 (15.2)	0.476
Pre-op LVEF (%); median (IQR)	60 (49 to 67)	64 (46 to 70)	0.600
Pre-op PEFR (mL/second); mean±SD	398±104	369 ±126	0.312
Pre-op PaO_2 (mmHg); median (IQR)	139 (109 to 162)	110 (96 to 152)	0.149
Pre-op $PaCO_2$ (mmHg); mean±SD	38.3±6.2	40.2±7.9	0.290
Pre-op PaO_2/FiO_2; median (IQR)	430 (326 to 506)	344 (299 to 475)	0.304
Bypass time (minute); mean±SD	144±56	130±47	0.304
Aortic cross clamp time (minute); mean±SD	99±47	80±28	0.054
Post-op LVEF (%); mean±SD	53±14	53±15	0.961
Intubation duration (hours); median (IQR)	15.3 (12.7 to 18.93)	13.4 (9.1 to 17.2)	0.156

CKD=chronic kidney disease; COPD=chronic obstructive pulmonary disease; ESRD=end-stage renal disease; FiO_2=fraction of inspired oxygen; HD=hemodialysis; HFNC=high-flow nasal oxygen cannula; IQR=interquartile range; IS=incentive spirometer; LVEF=left ventricular ejection fraction; NYHC=New York heart classification; $PaCO_2$=partial pressure of carbon dioxide; PaO_2=partial pressure of oxygen; PaO_2/FiO_2=ratio of arterial partial pressure of oxygen to fraction of inspired oxygen; PEFR=peak expiratory flow rate; SD=standard deviation

* Statistical significance, p≤0.05

median 3 days (IQR 2 to 3) in the IS group, p=0.245]. Prolonged ICU and hospital stay were associated with postoperative pneumonia. Patients in both groups showed a significant decrease in the PaO_2/FiO_2 of approximately 33.5% on day 1 and 26.4% on day 3 compared to the preoperative value. The PEFR also decreased to 62.5% on day 1 and 41.7% on day 3, and this was the same in both groups (Figure 2). The

Table 2. Primary and secondary outcomes

Variable	HFNC (n=34); median (IQR)	IS (n=33); median (IQR)	p-value
Postoperative complication			
Intervention failure; n (%)	10 (29.4)	8 (24.2)	0.784
Reintubation; n (%)	7 (20.6)	1 (3.0)	0.054
Time to reintubation (hours)	40.8 (8.5 to 45)	57.8 (57.8)	0.275
ICU stay (days)	3 (2 to 5)	3 (2 to 3)	0.245
Hospital stay (days)	9 (7 to 12)	8 (6 to 9)	0.010*
Postoperative day 1			
$PaCO_2$ (mmHg)	38 (34 to 41)	38 (34 to 40)	0.940
PaO_2/FiO_2	268 (188 to 312)	277 (214 to 339)	0.580
Pain score	5 (5 to 6)	5 (4 to 6)	0.284
PEFR (mL/second)	130 (90 to 200)	125 (80 to 170)	0.589
Postoperative day 2			
$PaCO_2$ (mmHg)	36 (35 to 41)	37 (33 to 41)	0.726
PaO_2/FiO_2	281 (204 to 384)	291 (232 to 392)	0.603
Pain score	4 (3 to 5)	4 (3 to 5)	0.664
PEFR (mL/second)	130 (90 to 200)	125 (80 to 170)	0.876
Postoperative day 3			
$PaCO_2$ (mmHg)	36 (35 to 41)	37 (33 to 41)	0.879
PaO_2/FiO_2	268 (188 to 312)	290 242 to 358)	0.652
Pain score	3 (2 to 3)	3 (2 to 4)	0.832
PEFR (mL/second)	210 (150 to 295)	210 (150 to 310)	0.663
Postoperative day 4			
Pain score	1 (0 to 3)	2 (0 to 3)	0.205
PEFR (mL/second)	255 (195 to 310)	250 (170 to 355)	0.809
Postoperative day 5			
Pain score	0.5 (0 to 2)	2 (0 to 2)	0.565
PEFR (mL/second)	299 (212 to 350)	295 (190 to 397)	0.920

FiO_2=fraction of inspired oxygen; HFNC=high-flow nasal oxygen cannula; IQR=interquartile range; IS=incentive spirometer; $PaCO_2$=partial pressure of carbon dioxide; PaO_2=partial pressure of oxygen; PaO_2/FiO_2=ratio of arterial partial pressure of oxygen to fraction of inspired oxygen; PEFR=peak expiratory flow rate

* Statistical significance, p≤0.05

$PaCO_2$ levels were 37.4±7.1 mmHg, 37.9±5.9 mmHg, and 37.4±6.8 mmHg on postoperative days 1, 2, and 3, respectively; the values were within the normal limits and did not differ between the two groups (p=0.805). The median pain score on day 1 was 5 points, and it decreased on the following day, indicating that patient activities were not limited by pain.

Discussion

The present study was a prospective randomized controlled trial compared the use of prophylactic HFNC and IS with normal breathing exercises within 24 hours of extubation with respect to the decrease in the reintubation rates in cardiac surgery patients. The authors found the rate of intervention failure within 24 hours did not differ between the two groups. In the HFNC group, the reintubation rate was actually higher (up to 20.6%) compared to 3% in the IS group, although this difference was not statistically significant (p=0.054). Hospital stays were longer in the HFNC group because the patients were re-intubated and 5.97% progressed to hospital-acquired pneumonia, which was a higher rate than that reported in other studies (3.5% to 54.3%)[8].

Patients who underwent cardiac surgery with median sternotomy showed a significantly decreased vital capacity, 6% to 13% of the preoperative value on pulmonary function tests for up to 4 months after the surgery[9], and chest movement seems to decrease, especially in the upper thoracic part[10]. Atelectasis

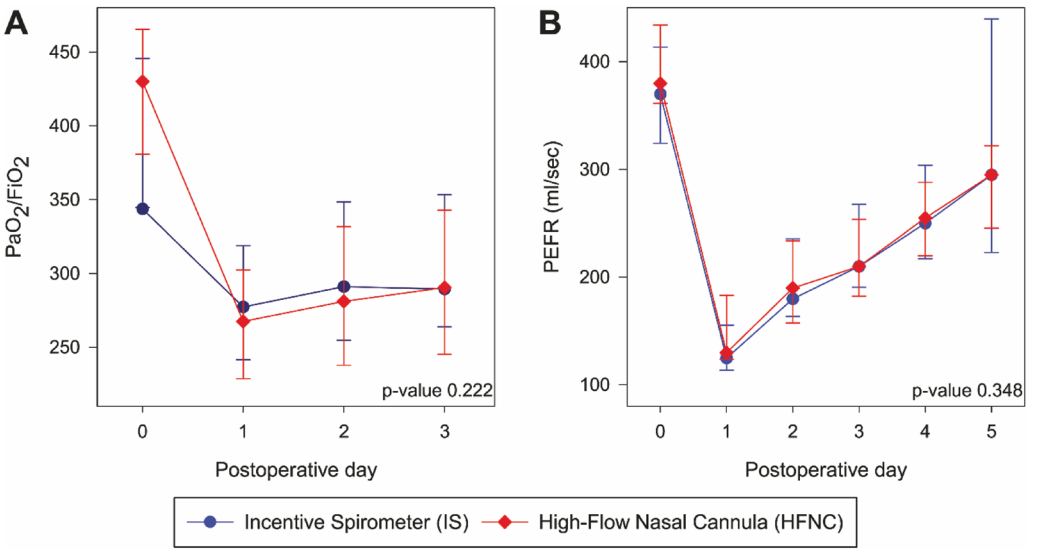

Figure 2. PaO_2/FiO_2 ratio and PEFR.

(A) On postoperative day 1, the PaO_2/FiO_2 ratio decreases by up to 33.5%, and (B) PEFR decreases by up to 62.5% from the preoperative value.
PaO_2/FiO_2=ratio of arterial partial pressure of oxygen to fraction of inspired oxygen; PEFR=peak expiratory flow rate

is the most common pulmonary complication aggravated by poor inspiratory effort, weak cough, pulmonary edema, and immobilization[11]. Positive airway pressure ventilation with a lung recruitment maneuver may improve atelectasis, but its effect and postoperative oxygenation are lost after extubation[12]. Reintubation is commonly performed within 24 hours after extubation in cardiac surgery patients[1]. The authors hypothesized that using prophylactic HFNC in addition to standard oxygen supplementation during this period may optimize respiratory care and reduce the rate of reintubation.

On using an HFNC, the anatomical naso-pharyngeal dead space is reduced due to high gas flushing flow, positive airway pressure is generated, and end-expiratory lung volume is increases[13], all of which reduce the breathing effort[14]. The user-friendliness of HFNC and the associated high level of patient tolerance increase its potential for clinical application. In non-surgical acute respiratory failure patients, treatment with HFNC, NIV, or standard oxygen supplementation does not result in different intubation rates[15], and a meta-analysis of 11 randomized controlled studies failed to report its superior efficacy in an adult ICU setting[16].

In a study involving high-risk cardiac surgery patients who had chronic lung diseases, were heavy smokers, or were morbidly obese (body mass index (BMI) ≥35 $kg.m^{-2}$), HFNC reduced the length of hospital stay and rate of ICU re-admission[17]. However, compared to NIV, the prophylactic use of HFNC in obese patients (BMI ≥30 $kg.m^{-2}$) did show significantly different clinical outcomes and rates of treatment failure[18]. After extubation, the reintubation rates were not significantly different between HFNC patients and those who received conventional oxygen therapy, among cardiac surgery patients[19]. In hypoxemic patients, HFNC was not inferior to intermittent NIV with respect to the prevention of respiratory failure, with a reintubation rate of approximately 14% in both groups[20]. The atelectasis scores on chest radiography, FVC, and FEV_1 were not different between patients treated with HFNC and those treated with usual care[21]. Evidence supporting the use of prophylactic HFNC for the prevention of pulmonary complications is very limited.

In theory, an IS promotes deep breathing efforts to improve pulmonary function, and IS is commonly used in hospitals. Despite this, a randomized controlled trial reported that at 2 months after cardiac surgery, patients who performed deep breathing exercises failed to show significantly superior improvements in lung function compared to patients who did not perform breathing exercises[22]. A recent systematic review reported no evidence that IS reduces the incidence of atelectasis and pulmonary complications in cardiac surgery patients[23,24]. In the authors' institute still use IS in combination with physical therapy as a part of the routine postoperative rehabilitation program since the authors believe that

full inspiration may promote efficient elimination of sputum. In the authors' experience, HFNC patients seem to cough less frequently and they complain of difficulty in breathing less frequently. The rate of pneumonia in the HFNC group was 11% in the present study, which necessitated reintubation. The authors could not find any studies report that HFNCs are associated with pneumonia, similar to ventilator assisted.

There were several limitations to the present study. First, the duration of HFNC insertion was limited to 24 hours postoperatively in line with the authors' hypothesis. In the real clinical setting, patients may need a more extended period of HFNC insertion to support the promotion of respiratory function, and a study with extended periods may report different results. Second, the authors did not obtain the full preoperative pulmonary function test results in the sample population, therefore, some patients may have had an impaired result or experienced further development of postoperative pulmonary complications. Third, the reintubation rate was higher in the HFNC group, but the difference in the rates was not statistically significant between the two groups. The authors suspect that the reintubation rate was higher in the HFNC group owing to the small sample size used to determine the p-value, and a multi-center study with a larger sample size should be undertaken.

Conclusion

Prophylactic HFNC 24 hours after cardiac surgery does not reduce the rate of reintubation compared to IS. Furthermore, an increased rate of reintubation was associated with prophylactic HFNC, however, the increase was not statistically significant. The decision to administer prophylactic HFNC support after extubation in cardiac surgery patients should be contemplated on an individual basis.

What is already known on this topic?

In high-risk cardiac surgery patients who had chronic lung diseases, were heavy smokers, or morbidly obese (BMI $\geq$35 $kg.m^{-2}$), HFNC reduced the length of hospital stay and rate of ICU re-admission.

What this study adds?

Prophylactic HFNC 24 hours after cardiac surgery does not reduce the rate of reintubation compared to conventional breathing exercise.

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Conflicts of interest

The authors declare no conflict of interest.

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