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High-Flow Nasal Cannula in the Immediate Postoperative Period

A Systematic Review and Meta-analysis

Dipayan Chaudhuri, MD; David Granton, BSc; Dominic Xiang Wang, BSc; Karen E. A. Burns, MD; Yigal Helviz, MD; Sharon Einav, MD; Vatsal Trivedi, MD; Tommaso Mauri, MD; Jean-Damien Ricard, MD; Jordi Mancebo, MD; Jean-Pierre Frat, MD; Sameer Jog, MD; Gonzalo Hernandez, MD; Salvatore M. Maggiore, MD; Lawrence Mbuagbaw, MD; Carol L. Hodgson, PhD; Samir Jaber, MD; Ewan C. Goligher, MD; Laurent Brochard, MD; and Bram Rochwerg, MD

BACKGROUND: Studies have demonstrated that high-flow nasal cannula (HFNC) prevents intubation in acute hypoxic respiratory failure when compared with conventional oxygen therapy (COT). However, the data examining routine HFNC use in the immediate postoperative period are less clear.

RESEARCH QUESTION: Is routine HFNC use superior to COT or noninvasive ventilation (NIV) use in preventing intubation in patients postoperatively?

STUDY DESIGN AND METHODS: We comprehensively searched databases (PubMed, Embase, Web of Science) to identify randomized controlled trials (RCTs) that compared the effect of HFNC use with that of COT or NIV in the immediate postoperative period on reintubation, escalation of respiratory support, hospital mortality, ICU and hospital length of stay (LOS), postoperative hypoxemia, and treatment complications. We assessed individual study risk of bias (RoB) by using the revised Cochrane RoB 2 tool and rated certainty in outcomes by using the Grading of Recommendations Assessment, Development and Evaluation framework.

RESULTS: We included 11 RCTs enrolling 2,201 patients. Ten compared HFNC with COT and one with NIV. Compared with COT use, HFNC use in the postoperative period was associated with a lower reintubation rate (relative risk [RR], 0.32; 95% CI, 0.12-0.88; absolute risk reduction [ARR], 2.9%; moderate certainty) and decreased escalation of respiratory support (RR, 0.54; 95% CI, 0.31-0.94; ARR, 5.8%; very low certainty). Post hoc subgroup analysis suggested that this effect was driven by patients who were obese and/or at high risk (subgroup differences, $P = .06$). We did not find differences in any of the other stated outcomes between HFNC and COT. HFNC was also no different from NIV in reintubation rate, respiratory therapy failure, or ICU LOS.

INTERPRETATION: With evidence of moderate certainty, prophylactic HFNC reduces reintubation and escalation of respiratory support compared with COT in the immediate postoperative period after cardiothoracic surgery. This effect is likely driven by patients who are at high risk and/or obese. These findings support postoperative prophylactic HFNC use in the patients who are at high risk and/or obese undergoing cardiothoracic surgery.

KEY WORDS: high-flow nasal cannula; meta-analysis; postoperative

Study Question: Is routine high-flow nasal cannula (HFNC) use superior to conventional oxygen therapy (COT) or noninvasive ventilation (NIV) in preventing intubation in patients postoperatively?

Results: Compared with COT use, HFNC use in the postoperative period was associated with a lower reintubation rate (RR, 0.32; 95% CI, 0.12-0.88; absolute risk reduction [ARR], 2.9%; moderate certainty) and decreased escalation of respiratory support (RR, 0.54; 95% CI, 0.31-0.94; ARR, 7.5%; very low certainty). Post hoc subgroup analysis suggested that this effect was driven by patients who were obese and/or at high risk (subgroup differences, $P = .06$).

Interpretation: Evidence of moderate certainty supports postoperative prophylactic HFNC use in the patient who is at high risk and/or obese who is undergoing cardiothoracic surgery.

Research Methods, Evidence and Impact (Drs Mbuagbaw and Rochwerg), McMaster University, Hamilton; the Schulich School of Medicine (Mr Wang), Western University, London; and the Interdepartmental Division of Critical Care Medicine (Drs Goligher and Brochard), University of Toronto, and the Keenan Research Centre for Biomedical Science (Dr Brochard), Li Ka Shing Knowledge Institute, St Michael's Hospital, Toronto, ON, Canada; the Department of Anaesthesiology and Critical Care Medicine B (DAR B) (Drs Burns, Trivedi, and Jaber), Saint-Eloi Teaching Hospital, PhyMed Exp, INSERM U1046, University of Montpellier, Montpellier; the Assistance Publique-Hôpital de Paris, Service de Réanimation Médico-chirurgicale (Dr Ricard), Hôpital Louis Mourier, Colombes; the Université de Paris, INSERM, IAME, UMR 1137, Paris; and the CHU de Poitiers, Médecine Intensive Réanimation (Dr Frat), Poitiers; the INSERM, CIC-1402, équipe ALIVE, Poitiers; and the Université de Poitiers, Faculté de Médecine et de Pharmacie de Poitiers, Poitiers, France; the General Intensive Care Unit (Drs Helviz and Einav), Shaare Zedek Medical Center, and the Faculty of Medicine (Dr Einav), Hebrew University, Jerusalem, Israel; the Dipartimento di fisopatologia medico-chirurgica e dei trapianti (Dr Mauri), Università degli Studi di Milano, and the Department of Anesthesia, Critical Care and Emergency, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, University of Milan, Milan; and the Department of Medical, Oral and Biotechnological Sciences (Dr Maggiore), Gabriele d'Annunzio University of Chieti-Pescara, and Department of Anesthesiology and Critical Care, SS. Annunziata Hospital, Chieti, Italy; the Servei de Medicina Intensiva (Dr Mancebo), Hospital Universitari Sant Pau, Barcelona, Spain; the Department of Intensive Care Medicine (Dr Jog), Deenanath Mangeshkar Hospital and Research Centre, Pune, India; the University Hospital Virgen de la Salud (Dr Hernandez), Toledo, Spain; and the Department of Epidemiology and Preventive Medicine (Dr Hodgson), Australian and New Zealand Intensive Care Research Centre, Monash University, Melbourne, VIC, Australia.

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Acute respiratory failure is one of the most common complications after cardiac or noncardiac surgery.[1-3] Postoperative respiratory failure, often due to atelectasis or pulmonary edema, is associated with increased mortality (as high as 27%),[1] increased ICU length of stay (LOS), longer rehabilitation, and poorer long-term functional outcomes.[4] Hypoxia and hypoxemia are common manifestations of postoperative respiratory failure.[5] Depending on patient phenotype and the type of surgery performed, rates of postoperative respiratory failure as high as 10% to 50% have been demonstrated.[1] Oxygen therapy administered with low-flow nasal cannula or Venturi mask typically is used in patients prophylactically after extubation postoperatively to prevent hypoxia. If respiratory failure develops and low-flow oxygen therapy fails, noninvasive ventilation (NIV) and/or invasive mechanical ventilation are instituted as the next step.[6-8] However, both NIV and invasive mechanical ventilation are resource intensive, are associated with patient discomfort, and present a high risk for complications.[9,10]

A high-flow nasal cannula (HFNC) enables delivery of heated and humidified oxygen at flow rates that more closely approximate the inspiratory needs of patients with dyspnea.[11] HFNC also provides a modest amount of positive end-expiratory pressure and decreases both pharyngeal dead space and nasopharyngeal resistance.[12,13] Furthermore, HFNC may be more comfortable and less obtrusive than other forms of oxygen delivery for patients.[13] Some studies, including a systematic review and meta-analysis performed by our group, have demonstrated that HFNC prevents intubation when compared with conventional oxygen therapy (COT) in acute hypoxic respiratory failure.[14] The data examining HFNC used in the postoperative period (within 24 h of surgery) are less clear.[15-17] We sought to conduct a systematic review and meta-analysis comparing HFNC with COT when used routinely in the immediate postoperative period.

Materials and Methods

We registered our protocol on PROSPERO (CRD42019147870). We report our findings by using a Preferred Reporting Items for Systematic Reviews and Meta-Analyses checklist (e-Table 1).

Data Sources and Searches

We performed a comprehensive search of relevant databases (PubMed, Embase, and Web of Science) from January 1, 2007 (because HFNC

was not widely used before this time) to April 15, 2019. We used keywords including "human" OR "adult" OR "mature" or "grown" AND "high flow nasal cannula" OR "high flow nasal therapy" OR "high flow nasal oxygen" OR "high flow oxygen therapy" OR "high flow therapy" OR "optiflow (respiration)" OR "nasal highflow". We did not exclude studies on the basis of language or trial quality. We updated the literature search on November 6, 2019.

Study Selection

Two independent reviewers (D. G., D. X. W.) screened all citations in duplicates in two stages by first examining the title and abstracts and then, for selected citations, the full texts. We captured reasons for study exclusion after reviewing the full texts of identified trials. A third reviewer (B. R.) adjudicated disagreements.

We included all randomized controlled trials (RCTs) that compared HFNC with other noninvasive oxygen delivery modalities (traditional nasal cannula, Venturi mask, NIV, and so on) in the immediate postoperative period. We included trials examining both cardiac and noncardiac surgery. We excluded case series, case reports, and observational studies. Our outcomes of interest included reintubation, escalation of respiratory therapy, hospital mortality, ICU LOS, hospital LOS, postoperative hypoxemia, and complications. Escalation of respiratory therapy was defined as escalation to NIV or mechanical ventilation for the HFNC arm and as escalation to HFNC, NIV, or mechanical ventilation for the COT arm. Reintubation was defined as intubation of the trachea within 48 hours after postoperative extubation in the ICU or the postanesthesia recovery room.

Data Extraction and Quality Assessment

Two independent reviewers (D. C., D. G., or D. X. W.), working in pairs, abstracted data in duplicate by using a standardized data abstraction form. A third reviewer (B. R.) adjudicated disagreements. We collected data on trial characteristics, demographic data, interventional and control details, and outcomes. We contacted individual trial authors for missing data.

We assessed risk of bias (RoB) in duplicate by using the revised Cochrane RoB 2 tool for RCTs.[18] We assessed each RCT by using the following domains: randomization process, deviations from intended interventions, missing outcome data, measurement of the outcome, and selection of the reported result. For each domain, we rated the RoB to be low, high, or some concerns on the basis of an algorithm that used signaling questions specific to each domain. The overall RoB for each trial was the highest risk attributed to any domain. Overall certainty of evidence was assessed for each outcome by using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) framework.[19]

Data Analysis

We used the DerSimonian-Laird random-effects model with inverse-variance weighting to generate pooled treatment effects across studies. Heterogeneity between trials was assessed using a combination of the χ^2 test, the I^2 statistic, and visual inspection of the forest plots.[20] We present results of dichotomous outcomes by using relative risk (RR) and continuous outcomes as mean difference (MD), both with 95% CIs. We also provide absolute differences with 95% CIs. We performed all statistical analysis by using software (RevMan 5.3; Cochrane Collaboration).

We planned four a priori subgroup analyses: (1) patients after cardiac surgery vs patients not undergoing cardiac surgery, (2) patients at high risk of respiratory failure (as defined by the investigators in each trial) vs those at low risk of respiratory failure, (3) patients who were obese vs patients who were not obese, and (4) high-RoB studies vs low-RoB studies. A priori, we hypothesized that patients at high risk who were undergoing cardiac surgery, patients who were obese, and trials at high RoB would show greater benefit with HFNC therapy. We also performed a post hoc subgroup analysis in which we combined patients at high risk of respiratory failure and patients who were obese as an overall high-risk subgroup. We hypothesized that this subgroup would show greater benefit with HFNC therapy.

We conducted trial sequential analysis[21] by using the random-effects model for trials reporting reintubation. For this analysis, we used a statistical significance level of 5%, a power of 80%, and an RR reduction of 15% to represent a clinically important difference. We used a model variance-based heterogeneity correction. We performed trial sequential analysis by using software (Trial Sequential Analysis version 0.9.5.10 beta; Copenhagen Trial Unit, Center for Clinical Intervention Research, Rigshospitalet; www.ctu.dk/tsa).

Results

Search Strategy and Study Characteristics

We reviewed 650 citations and included 11 RCTs (n = 2,201) after screening (Fig 1).[5,15-17,22-28] We excluded one RCT that compared HFNC with a high-flow face mask (with use of minimum flows of 15 L/min) because this comparator was judged to be an alternative delivery system and very similar to HFNC.[29]

Table 1 shows the characteristics of the included RCTs, which randomly assigned between 51 and 830 patients. Only one RCT compared HFNC with NIV.[15] The remaining trials compared HFNC with COT. NIV was too different as a comparator to pool with COT, so we did not include this trial in the quantitative analysis. Six of the 11 RCTs were conducted in patients after cardiac surgery[15,17,22,24-26]; of the remaining five, four were conducted in patients after thoracic surgery,[16,23,27,28] and one was conducted in patients after major thoracic and abdominal surgery.[5]

Four of the included studies examined patients at moderate to high risk of postoperative respiratory complications.[5,15,26,28] In two of the RCTs, this was defined as an Assess Respiratory Risk in Surgical Patients in Catalonia score ≥ 26,[5,28] with the maximum possible score being 123 and a sigmoid relationship between score and risk. In the third trial, examining patients after cardiac surgery, high risk was defined as any patient having at least one risk factor for postoperative pulmonary complications, including history of COPD, asthma, lower respiratory tract infection in the preceding 4 weeks, a BMI ≥ 35 kg/m^2,

or current (within last 6 week) heavy smokers (> 10 pack-years)].[26] The fourth trial included only patients after cardiac surgery who were deemed to be at risk for needing postoperative oxygen therapy on the basis of predefined risk factors, including BMI > 30 kg/m^2, left ventricular ejection fraction < 40%, and a previous failed extubation (Table 1).[15] Two trials examined patients who were obese exclusively,[17,25] whereas two RCTs specifically excluded people who were obese.[5,27] All trials, except for the RCT that used NIV as a comparator,[15] used HFNC prophylactically rather than as a treatment for respiratory failure.

Nine RCTs[5,15,17,23-28] used one device (Optiflow; Fisher & Paykel Healthcare), and one trial used another device (MaxVenturi; Maxtec, LLC).[16] Another trial[22] did not specify the type of HFNC device used. All HFNC devices provided heated and humidified nasal oxygen at high flows titrated between 25 and 60 L/min, with the goal of keeping the patient comfortable and aiming for an oxygen saturation as measured by pulse oximetry (Spo_2) target > 90%.

e-Table 2 summarizes the RoB for each trial. None of the trials blinded patients or physicians. Given that all our outcomes were hard end points, we thought that there was unlikely to be clinically significant RoB from lack of blinding. Thus, all trials except one[16] were judged to be at low RoB.

Outcomes

Reintubation or Need for Escalation: In e-Table 3, we depict the GRADE certainties and pooled estimates for pooled outcomes. Compared with COT use, HFNC use in the immediate postoperative period significantly decreased the need for reintubation (900 patients in six trials; RR, 0.32; 95% CI, 0.12–0.88; absolute risk reduction [ARR], 2.9%; 95% CI, 0.5%-3.7% reduction; moderate certainty) (Fig 2). The reintubation rate was 0.9% (four of 454) in the HFNC group and 4.3% (19 of 446) in the COT group. The trial sequential analysis for this outcome showed that the required information size (n = 28,364) was not met, and, consequently, we rated down the certainty for this outcome on the basis of imprecision. HFNC use was also associated with a significant decrease in the need for escalation of respiratory support (RR, 0.54; 95% CI, 0.31-0.94; ARR, 5.8%; 95% CI, 2.1%-9.5% reduction) (Fig 3) with evidence of very low certainty.

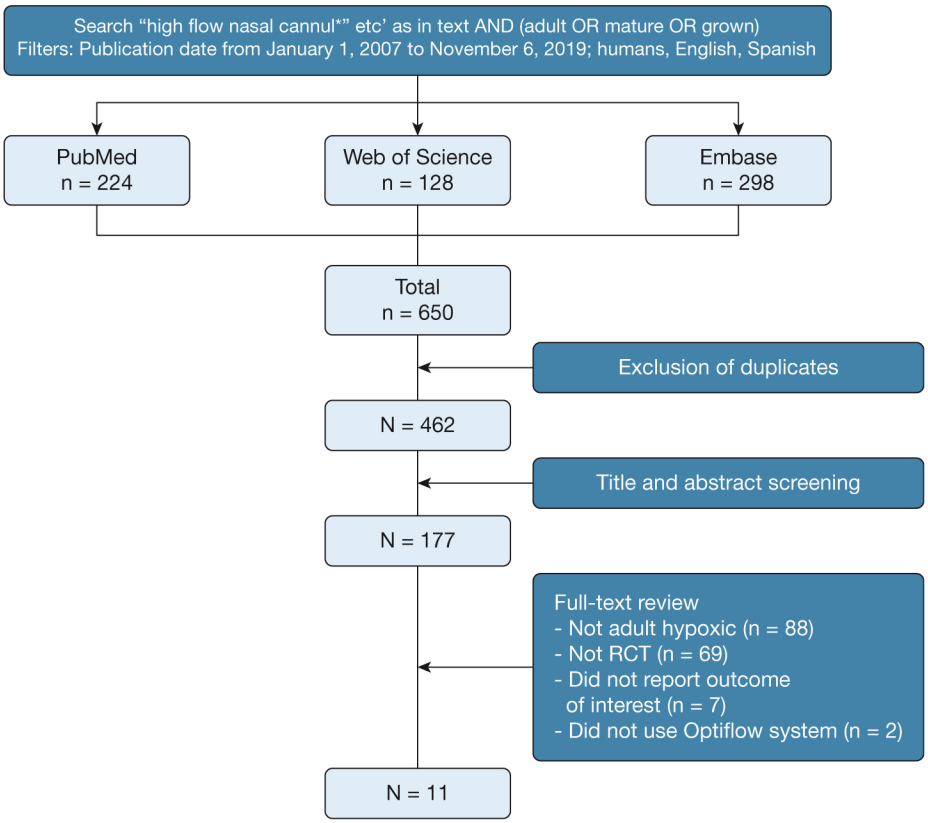

Figure 1 – *Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow diagram of study selection. RCT = randomized controlled trial.*

TABLE 1] Characteristics of Included Studies

Study/Year	Country	No. of Patients Randomly Assigned	Population	Intervention Details	Comparator Details	Outcomes
Ansari et al[23]/ 2016	Cambridge, United Kingdom	59	Inclusion: Elective lung resection surgery, and age > 18 y Exclusion: Pneumonectomy, contraindication to HFNC, and mobilization limitation leading to inability to perform 6MWT	(Optiflow; Fisher & Paykel Healthcare) Flow: Started at 50 L/min and titrated to saturations and comfort Duration: First 24 h	Simple face mask or nasal prongs at 2to 4 L/min Duration: 24 h and then as needed	Hospital LOS, 6MWT, difference between preoperative and postoperative FEV_1
Brainard et al[16]/ 2017	Aurora, Colorado, United States	51	Inclusion: > 18 y of age undergoing thoracic surgery with scheduled admission to the ICU postoperatively Exclusion: Pregnant or breastfeeding, OSA, lung transplant, previous pneumonectomy, home oxygen > 4 L/min, or inability to adhere to assigned treatment for the intended duration	(MaxVenturi; Maxtec LLC) Flow: Started at 40 L/min and titrated to saturations and comfort Duration: First 48 h or discharge from ICU	Nasal cannula or face mask oxygen Duration: First 48 h or discharge from ICU	Postoperative pulmonary complications (composite of severe hypoxemia, $Spo_2 < 90\%$ with $Fio_2 \geq 50\%$), acute respiratory failure, escalation of therapy to NIV, reintubation, occurrence of hospital-acquired pneumonia (or readmission to the ICU), ICU LOS, hospital LOS
Corley et al[17]/ 2015	Brisbane, Australia	155	Inclusion: > 18 y with a BMI > 30 kg/m^2 and scheduled to undergo cardiac surgery or cardiopulmonary bypass Exclusion: Ventilation time > 36 h, extubation onto NIV, requirement for tracheostomy, and extubation as part of end-of-life treatment	(Optiflow; Fisher & Paykel Healthcare) Flow: Started at 35 L/min and titrated to saturations and comfort Duration: 8 h minimum and longer if needed	Simple face mask or nasal prongs Duration: 8 h or longer as needed	ICU LOS, escalation of respiratory therapy, reintubation, average PF ratio in first 24 h
Futier et al[5]/ 2016	France	220	Inclusion: All adult patients scheduled for abdominal, or abdominal and thoracic surgery with an anticipated duration of 2 h or more and an ARISCAT risk score of 26 points or more, were eligible for recruitment	(Optiflow; Fisher & Paykel Healthcare) Flow: Started at 50 L/min and titrated to	Nasal prongs or face mask Duration: First 24 h	Hospital mortality, hypoxia, ICU LOS, hospital LOS, escalation of respiratory support, reintubation, complications

(Continued)

TABLE 1] *(Continued)*

Study/Year	Country	No. of Patients Randomly Assigned	Population	Intervention Details	Comparator Details	Outcomes
			Exclusion: BMI > 35 kg/m^2, life-threatening condition requiring emergency surgery, OSA syndrome, and pregnancy	saturations and comfort Duration: First 24 h		
Parke et al[24]/ 2013	Auckland, New Zealand	341	Inclusion: Adult patients with elective cardiac surgery using cardiopulmonary bypass Exclusion: Contraindication to HFNC if participants had not met the extubation criteria by 10 am the day after surgery	(Optiflow; Fisher & Paykel Healthcare) Flow: Started at 45 L/min and titrated to saturations and comfort Duration: First 48 h	Simple face mask or nasal prongs Duration: First 48 h	28-day mortality, ICU LOS, hospital LOS, escalation of respiratory care, reintubation, postoperative FEV_1
Pennisi et al[27]/ 2019	Rome, Italy	96	Inclusion: All adult patients scheduled for elective thoracotomic pulmonary lobar resection for malignant disease Exclusion: Pregnancy, BMI ≥ 35 kg/m^2, history of OSA syndrome, long-term oxygen therapy because of chronic pulmonary disease, tracheostomy, and any nasal or facial defect that could impede HFNC or Venturi mask use	(Optiflow; Fisher & Paykel Healthcare) Flow: 50 L/min Duration: First 48 h	Venturi mask (OS/60 K; FIAB) Duration: First 48 h	ICU LOS, hospital LOS, escalation of respiratory therapy, reintubation, average PF ratio in first 48 h, hypoxia
Sahin et al[25]/ 2018	Istanbul, Turkey	100	Inclusion: All adult patients undergoing CABG with BMI > 30 kg/m^2 Exclusion: Hemodynamic instability, patients with tracheostomy, OSA, active pulmonary disease, known low cardiac output, and emergency surgery	(Optilfow; Fisher & Paykel Healthcare) Flow: Started at 25 L/min and titrated to oxygen saturation and comfort Duration: First 48 h	Simple face mask Duration: First 48 h	Hospital mortality, ICU LOS, hospital LOS, escalation of respiratory therapy, reintubation, postoperative day 2 FEV_1, complications
Stéphan et al[15]/ 2015	France	830	Inclusion: All adult patients undergoing cardiothoracic surgery and meeting any of the following criteria:	(Optiflow; Fisher & Paykel Healthcare) Flow: Started at	Bilevel pressure ventilation with full face mask Settings: 8/4 and	ICU mortality, ICU LOS, hospital LOS, escalation of respiratory therapy, reintubation, dyspnea score, comfort

(Continued)

TABLE 1] *(Continued)*

Study/Year	Country	No. of Patients Randomly Assigned	Population	Intervention Details	Comparator Details	Outcomes
			(1) failure of a spontaneous breathing trial, defined as $Sa_{O_2} < 90\%$ with 12 L of oxygen during a T-tube trial or $Pa_{O_2} < 75$ mm Hg with an F_{IO_2} of at least 50% during low-level pressure support (2) successful spontaneous breathing trial with any of the following preexisting risk factors: BMI < 30 kg/m^2, left ventricular ejection fraction $< 40\%$, and failure of previous extubation (3) successful spontaneous breathing trial followed by failed extubation, defined as at least one of the following: PF ratio < 300, respiratory rate > 25 breaths per minute for at least 2 h, and use of accessory respiratory muscles or paradoxical respiration Exclusion: OSA, tracheostomy, do-not-intubate status, delirium, nausea and vomiting, bradypnea, impaired consciousness, and hemodynamic instability	50 L/min and titrated to saturations and comfort Duration: Until $Sa_{O_2} > 95\%$ on 6 L/min or PF $>$ 300	titration to adequate volumes and comfort Duration: Until fewer than 4 h/d of bilevel pressure ventilation were needed	score, pneumonia, pneumothorax, colonic pseudo-obstruction
Tatsuishi et al[22]/2019	Tokyo, Japan	148	Inclusion: All adult patients undergoing off-pump CABG Exclusion: Concomitant procedures such as valve surgery or aortic surgery, chronic kidney disease, uncomfortable with HFNC	HFNC (company not specified) Flow: 45 to 60 L/min Duration: Until the end of postoperative day 1	Simple face mask with humidification Duration: Until the end of postoperative day 1	Loss of lung volume, duration and amount of oxygen therapy, postoperative diuretic use, ICU LOS, hospital LOS
Yu et al[28]/2017	Shanghai, China	110	Inclusion: Patients who underwent planned thoracoscopic lobectomy because of lung tumor with ARISCAT score > 26 Exclusion: Immunocompromised, pregnant, converted to an open thoracotomy because of poor	(Optiflow; Fisher & Paykel Healthcare) Flow: Started at 35 L/min, then titrated to saturations	Nasal prongs or face mask Duration: First 72 h	ICU LOS, hospital LOS, hypoxia, escalation of respiratory therapy, reintubation, mean PF ratio in first 48 h, complications

(Continued)

TABLE 1] *(Continued)*

Study/Year	Country	No. of Patients Randomly Assigned	Population	Intervention Details	Comparator Details	Outcomes
			visualization or bleeding, or > 80 y of age	and comfort Duration: First 72 h		
Zochios et al[26]/ 2018	Birmingham, United Kingdom	100	Inclusion: Elective cardiac surgery. aged > 18 y with one or more patient-related risk factors for postoperative pulmonary complications (COPD, asthma, lower respiratory tract infection in preceding 4 wk, BMI ≥ 35 kg/m^2, current heavy smokers), and capable of performing 6MWT Exclusion: Patients in whom high-flow nasal oxygen was contraindicated, those who needed CPAP preoperatively, or those who did not meet tracheal extubation criteria by 10 am the day after surgery postoperative day 1	(Optiflow; Fisher & Paykel Healthcare) Flow: Started at 30 L/min and titrated to saturations and comfort Duration: First 24 h	Nasal prongs or a soft face mask Duration: First 24 h	Hospital mortality, ICU LOS, hospital LOS, complications, escalation of respiratory care, reintubation, postoperative day 1 FEV_1, postoperative 6MWT

6MWT = 6-min walk test; ARISCAT = Assess Respiratory Risk in Surgical Patients in Catalonia; CABG = coronary artery bypass graft; HFNC = high-flow nasal cannula; LOS = length of stay; NIV = noninvasive ventilation; PF = Pa_{O_2}:F_{IO_2}; Sa_{O_2} = arterial oxygen saturation; Sp_{O_2} = oxygen saturation as measured by pulse oximetry.

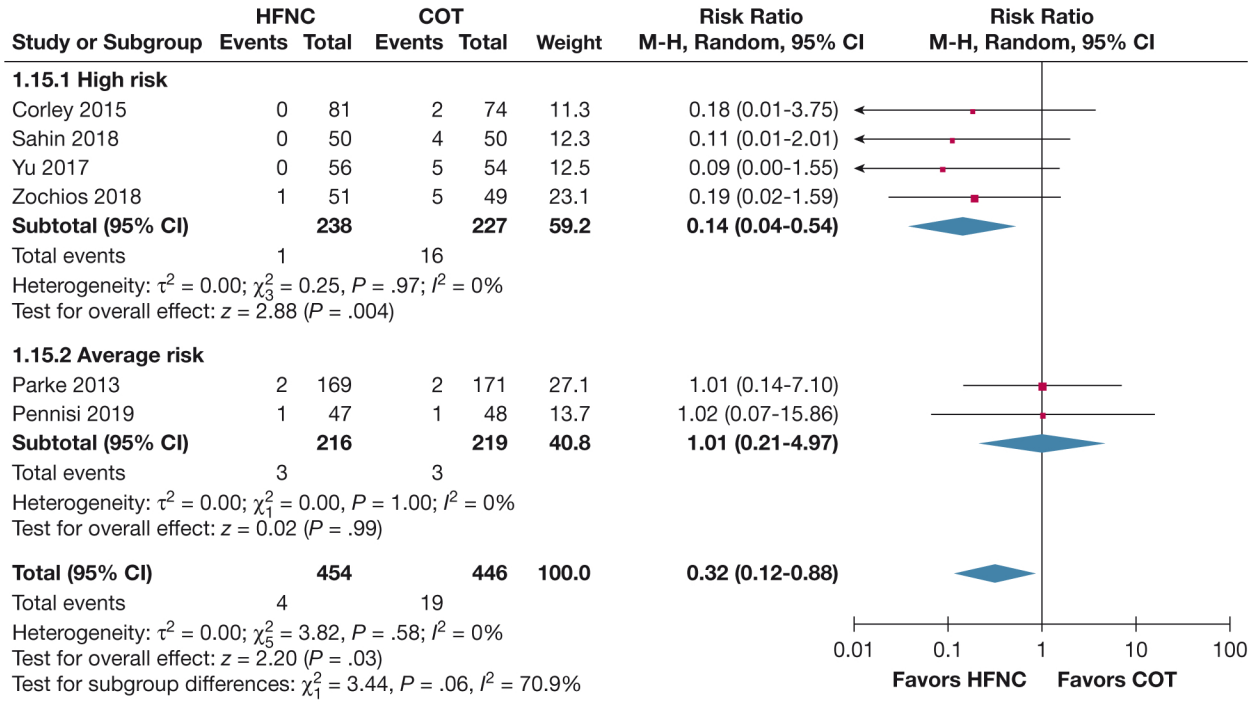

Figure 2 – *Effect of HFNC on reintubation rate when compared with conventional oxygen therapy. Studies are grouped by high risk (obese and/or at high risk of postoperative respiratory complications) and average risk. COT = conventional oxygen therapy; HFNC = high-flow nasal cannula; M-H = Mantel-Haenszel.*

Other Outcomes of Interest: We did not find a difference between HFNC and COT on other outcomes, including hospital mortality (RR, 0.64; 95% CI, 0.19-2.14; ARR, 0.7%; 95% CI, 1.5% reduction to 2.1% increase; low certainty) (Fig 4), ICU LOS (MD, 0.04 days higher; 95% CI, 0.11 days lower to 0.19 days higher; high certainty) (e-Fig 1), hospital LOS (MD, 0.43 days lower; 95% CI, 0.82 days lower to 0.04 days lower; moderate certainty) (e-Fig 2), and the incidence of postoperative hypoxemia (RR, 0.94; 95% CI, 0.79-1.13; ARR, 2.9%; 95% CI, 10% reduction to 6.2% increase; low certainty) (e-Fig 3). Postoperative hypoxia was variably defined among the included trials, with two trials defining it as $Spo_2 < 93\%$,[5,24] whereas others defined it based on a Pao_2:Fio_2 ratio < 300.[27,28]

Complications were heterogeneously reported across trials and were not amenable to pooling. We summarize complications in e-Table 4.

NIV Comparator: Compared with NIV, HFNC showed no difference in reintubation rate ($P = .99$) or the rate of respiratory therapy failure (absolute difference, 0.9%; 95% CI, −4.9% to 6.6%; $P = .003$). Although we did not find a difference in ICU LOS, we noted that skin breakdown was more common with NIV after 24 hours ($P < .001$).

Subgroup and Sensitivity Analysis: Subgroup analysis based on the type of surgery, risk of postoperative respiratory complications, and obesity did not show credible subgroup effects for any outcomes of interest (e-Figs 4-9). However, the post hoc high-risk subgroup consisting of patients who were obese and patients at high risk of postoperative respiratory complications showed a significant subgroup effect, with the high-risk group showing clear benefit in reintubation risk, whereas the average-risk group did not (high-risk group: RR, 0.14; 95% CI, 0.04-0.54; average-risk group: RR, 1.01; 95% CI, 0.21-4.97; test for subgroup differences: $P = .06$; $I^2 = 70.9\%$) (Fig 2). We also performed two post hoc sensitivity analysis excluding (1) two trials that excluded patients who were obese[5,27] and (2) one trial that focused on patients undergoing thoracoabdominal surgery.[5] The former was done to ensure that inclusion of studies with only patients at low risk (nonobese) did not lead to underestimation of the outcomes. The latter was done to exclude the only study that examined patients undergoing abdominal surgery to ensure that the generalizability of our conclusions was consistent for cardiac and thoracic surgery. Neither sensitivity analysis changed the overall results or conclusions. We performed a final sensitivity analysis by using the Paule-Mandel/empirical Bayes approach to pool treatment

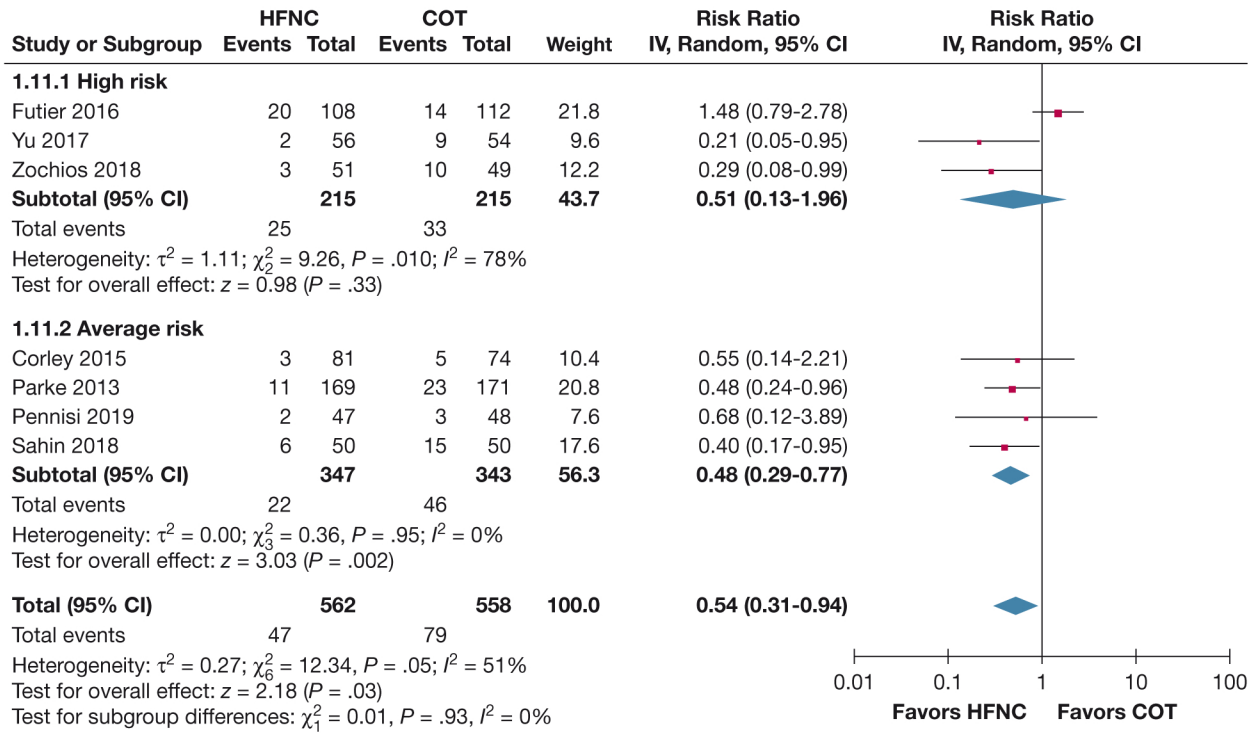

Figure 3 – *Effect of HFNC on escalation of respiratory support when compared with conventional oxygen therapy. Studies are grouped by high risk (obese and/or at high risk of postoperative respiratory complications) and average risk. IV = inverse variance. See Figure 2 legend for expansion of other abbreviations.*

effects for the three most critical outcomes (reintubation rate, escalation of respiratory support, and mortality) to ensure the robustness of our results. This analysis did not change the overall results or conclusions of this review (e-Figs 10-12).

Discussion

The typical patient behaves differently postoperatively from those with critical illness because they usually are previously well, do not have structural lung disease, and typically are intubated to facilitate anesthesia and surgery. Our findings show that HFNC, when used in the immediate postoperative period, is associated with significant reductions in reintubation and escalation of respiratory support when compared with COT in patients undergoing cardiothoracic surgery who are at high risk (Figs 2, 3). However, there were no significant effects on other important clinical outcomes, including mortality, ICU LOS, and hospital LOS. Only one trial compared HFNC with NIV and demonstrated comparable effects on outcomes.

Unlike patients who are critically ill, patients undergoing cardiac surgery undergo planned extubation immediately after surgery or within a few hours after

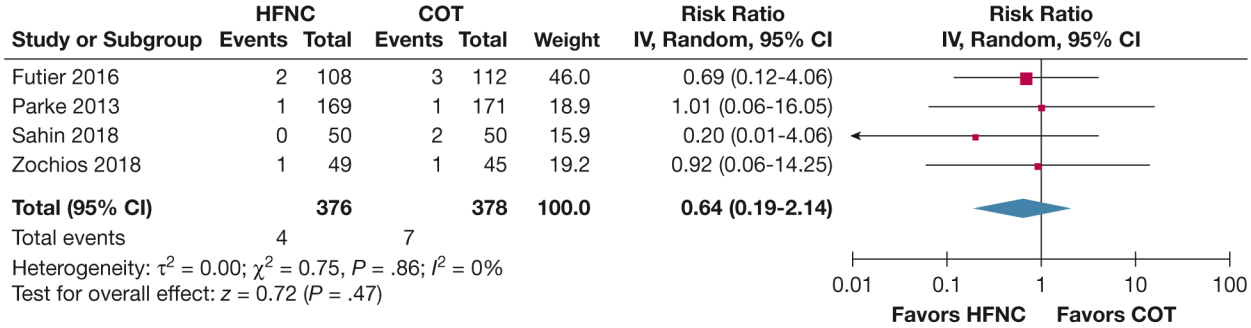

Figure 4 – *Effect on HFNC on mortality when compared with conventional oxygen therapy. See Figures 2 and 3 legends for expansion of abbreviations.*

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surgery.[30] Patients who develop respiratory failure in the postoperative period and require reintubation have significantly higher mortality, ICU LOS, hospital LOS, and costs.[31,32] When COT fails in a patient postoperatively or the patients is deemed to be at high risk for failure, most physicians consider using NIV in these patients to prevent reintubation.[6-8] However, NIV may be poorly tolerated, can cause skin breakdown, and often requires admission to a monitored setting such as surgical step-down unit or ICU.[15] HFNC is often better tolerated and may not require the same level of monitoring as NIV.[15] Stéphan et al[15] showed that in patients undergoing cardiothoracic surgery, HFNC did not increase the rate of escalating respiratory support or reintubation postoperatively compared with the rate with NIV. Therefore, prophylactic use of HFNC immediately after extubation postoperatively may prevent reintubation without requiring the level of care that is necessitated by NIV use.

Of the trials included in this review, all but one[5] exclusively examined patients undergoing major cardiac or thoracic surgery. Because intrathoracic surgery has the highest risk of postoperative pulmonary complications,[33] it stands to reason that this patient population is most likely to benefit from HFNC after extubation. Although upper abdominal surgery also carries a high risk of pulmonary complications,[33] the trial by Futier et al[5] did not show differences in treatment effect between patients treated with HFNC and patients treated with COT. Therefore, although our pooled analysis demonstrated potential benefit in all surgical types, the usefulness of HFNC after upper abdominal surgery remains uncertain.

Although previous meta-analyses have examined HFNC use in this population and found inconsistent results, we believe this may partly be explained by clinical heterogeneity. One previous meta-analysis[34] examined only patients undergoing cardiac surgery, excluding those undergoing thoracic or abdominal surgery. Conversely, another[35] included all patients after extubation (both critically ill and postoperative), thus combining different patient populations. Two other meta-analysis examined HFNC use in patients postoperatively and reported similar reductions in escalation of respiratory therapy and reintubation rates.[36,37] However, since the publication of these meta-analyses, five new RCTs have been published.[22,23,25-27] Moreover, one meta-analysis pooled both observational studies and RCTs together, a practice that has been questioned,[36] whereas the other included only four RCTs[37] and did not include seven additional eligible RCTs[5,15,22,23,25-27] that have been published since. In addition, neither systematic review preregistered their protocol. Our meta-analysis includes data from all published RCTs on this topic and thus, to our knowledge, is the most comprehensive analysis of current trial data. Strengths of our study include the comprehensive search, topic preregistration, and assessment of certainty by using the GRADE approach.

Our review also has limitations. First, the included trials studied heterogeneous populations; however, when possible, we performed subgroup analysis by type of surgery (cardiac surgery vs noncardiac surgery), level of risk (patients at high risk vs patients at average risk), and obesity. To this end, statistical heterogeneity was generally low, and none of the subgroups demonstrated credible effects, suggesting the importance of the clinical heterogeneity may be limited. Second, all included trials were, by necessity, unblended, which may have influenced individual trial results. Finally, although more than 2,000 patients were included in this review, the event rate for most of the outcomes of interest was low, resulting in imprecision in the pooled results.

Because the included trials examined only cardiothoracic and major abdominal surgery, the effect of using HFNC postoperatively in other patients undergoing surgery who are at risk of respiratory failure (neurosurgery; ear, nose, and throat surgery; or major vascular surgery) remains unknown.[38] Given that HFNC is likely most beneficial in high-risk surgeries, HFNC use in other patient populations and settings requires investigation. Similarly, further study is also needed to examine the role of NIV postoperatively in patients compared with HFNC alone or in combination with HFNC.

Interpretation

HFNC likely prevents reintubation and escalation of respiratory therapy, while having no significant effect on mortality or LOS, compared with COT in the immediate postoperative period in patients undergoing cardiothoracic surgery. The evidence is of moderate certainty. These findings support prophylactic use of HFNC in the population of patients requiring cardiothoracic surgery, particularly in patients who are at high risk and/or obese.

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Additional information: The e-Figures and e-Tables can be found in the Supplemental Materials section of the online article.

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