Management of Postoperative Hypoxemia

Kai Liu, J Brady Scott, Guoqiang Jing, and Jie Li

Hypoxemia is common in postoperative patients and is associated with prolonged hospital stays, high costs, and increased mortality. This review discusses the postoperative management of hypoxemia in regard to the use of conventional oxygen therapy, high-flow nasal cannula oxygen therapy, CPAP, and noninvasive ventilation. The recommendations made are based on the currently available evidence. *Key words: postoperative hypoxemia; oxygen therapy; high-flow nasal cannula; continuous positive airway pressure; noninvasive ventilation; incentive spirometry.* [Respir Care 2021;66(7):1136–1149.

Introduction

Hypoxemia is common in postoperative patients and mainly caused by atelectasis, ventilation/perfusion mismatch, or pulmonary edema. Postoperative hypoxemia is associated with increased mortality, prolonged hospital stays, and increased costs, especially in patients who have multiple risk factors.[1-4] Patients at risk often face prolonged respiratory support and re-intubation, which leads to poor overall outcomes. There is current evidence that early identification of risk factors of postoperative hypoxemia is imperative for the prevention or treatment of the condition. The purpose of this paper is to discuss pertinent findings from recent publications that pertain to postoperative management of hypoxemia. The recommendations are made based on the current evidence (Fig. 1).

Incidence and Outcome of Postoperative Hypoxemia

The incidence of postoperative hypoxemia ranges from 3% to 65%, depending on definitions, the presence of risk factors, and type of surgery.[2,4-6] Postoperative hypoxemia was variably defined in the publications included in this review. Definitions were a peripheral capillary oxygen saturation (S_{pO_2}) value of <93% on room air, or the ratio of the P_{aO_2}/F_{IO_2} of < 300 mm Hg.[7] Severe postoperative hypoxemia was defined as the need for an F_{IO_2} of 1.0 to maintain $S_{pO_2} \geq 85\%$.[8] However, recorded S_{pO_2} values might underestimate the severity of postoperative hypoxemia if

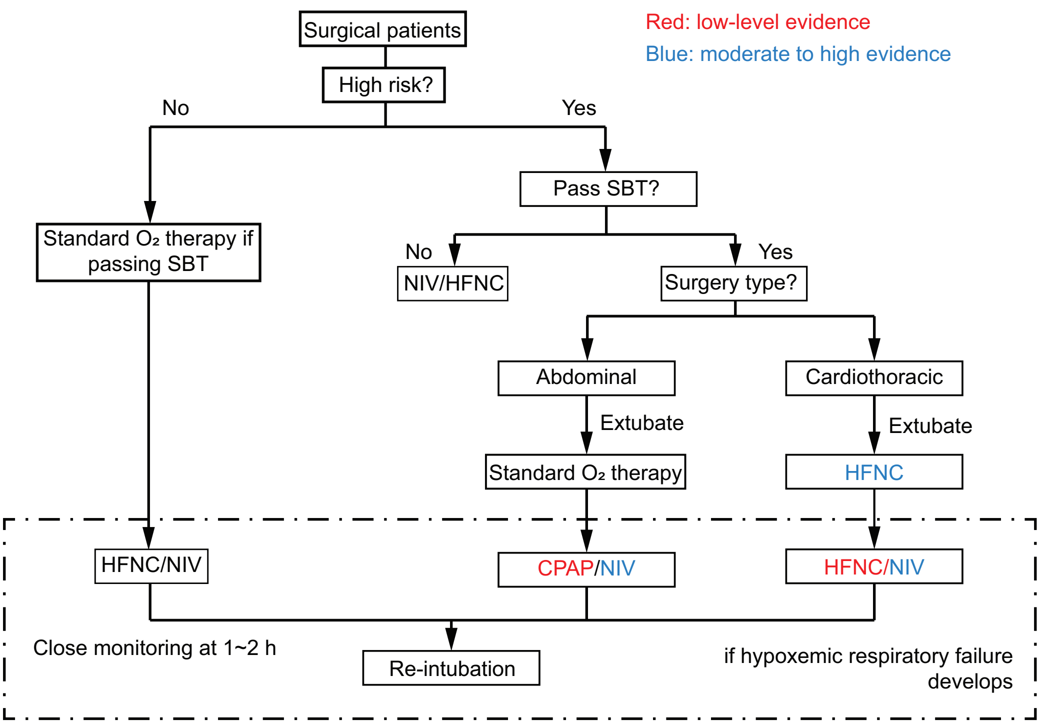

Fig. 1. Algorithm for respiratory support in postoperative patients. SBT = spontaneous breathing trial; NIV = noninvasive ventilation; HFNC = high-flow nasal cannula.

done manually and periodically. Sun et al[9] used the S_{pO_2} data that were recorded by a monitor at 1-min intervals in 833 postoperative adult subjects. More than one-fifth of the subjects in their study were found to have a $S_{pO_2} < 90\%$ for >10 min/h.[9] The inconsistent use of definitions in research papers and variable practices that relate to pulse oximetry complicates the understanding of the incidence of postoperative hypoxemia.

Postoperative hypoxemia has been reported to compromise wound healing and cause other severe complications, such as brain dysfunction, dysrhythmias, and myocardial ischemia. These complications are particularly noted within the first week after surgery. Of the 1,202 subjects with abdominal, orthopedic, and neurologic procedures reported by Fernandez-Bustamante et al,[10] 19.6% required prolonged oxygen therapy, whereas 17.1% developed atelectasis. These subjects also had significantly more ICU admissions, a longer ICU and/or hospital stay, and higher early mortality. Moderate and severe postoperative hypoxemia within the first 3 postoperative days has also been shown to be independently associated with increased postoperative mortality at 1 year.[4] Therefore, prevention and management of postoperative hypoxemia is necessary to improve patient outcomes.

Etiologies and Risk Factors of Postoperative Hypoxemia

The etiologies of postoperative hypoxemia include reduced chest wall and diaphragmatic activity caused by surgical-site pain, hemodynamic impairment, and anesthetic drugs. These factors may lead to ventilation/perfusion mismatch and alveolar hypoventilation.[11] Risk factors for postoperative hypoxemia are generally categorized as patient related or surgery related (Fig. 2). Understanding and identifying these risk

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Mr Liu is affiliated with the Department of Critical Care Medicine, Zhongshan Hospital, Fudan University, Shanghai, China. Dr Scott and Dr Li are affiliated with the Division of Respiratory Care, Department of Cardiopulmonary Sciences, Rush University, Chicago, Illinois. Mr Jing is affiliated with the Department of Pulmonary and Critical Care Medicine, Binzhou Medical University Hospital, Binzhou, Shandong, China.

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Correspondence: Jie Li PhD RRT RRT-ACCS RRT-NPS FAARC, Division of Respiratory Care, Department of Cardiopulmonary Sciences, Rush University, 600 S Paulina St, Suite 765, Chicago, IL 60612. E-mail: jie_li@rush.edu.

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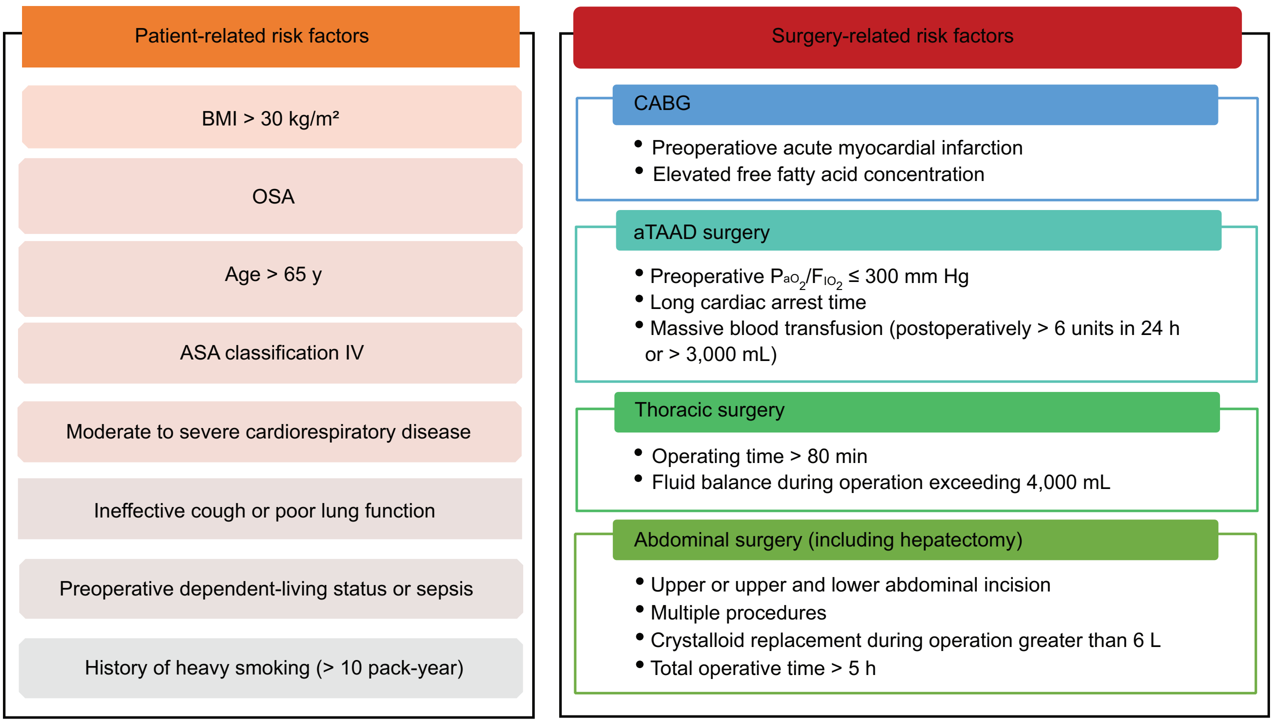

Fig. 2. Risk factors of postoperative hypoxemia. BMI = body mass index; OSA = obstructive sleep apnea; ASA = American Society of Anesthesiology; CABG = coronary artery bypass grafting; aTAAD = acute Stanford A aortic dissection.

factors can aid in the selection of appropriate respiratory care interventions.

Patients who are morbidly obese, with a body mass index (BMI) > 30 kg/m^2, experience more frequent oxygen desaturation episodes after surgery compared with patients with normal weight.[12] Patients with obstructive sleep apnea are at high risk of developing postoperative hypoxemia due to hypoventilation.[13] These subjects with a preoperative apnea-hypopnea index of ≥ 15 were reported to be independently associated with postoperative hypoxima.[14] Other patient-related risk factors include being elderly (generally > 65 years), an American Society of Anesthesiology physical status classification of IV, a preoperative dependent-living status, preoperative sepsis, moderate-to-severe cardiorespiratory disease, ineffective cough or poor lung function, and history of heavy smoking (>10 pack-years).[15]

In general, high-risk surgeries that are associated with the development of postoperative hypoxemia include brain, aortic, cardiac, thoracic, and upper abdominal surgery.[2] In addition to the surgical procedures themselves, other risk factors contribute to the development of hypoxemia. Preoperative acute myocardial infarction and elevated free fatty acid concentrations are risk factors of postoperative hypoxemia after a coronary artery bypass grafting procedure.[16-19] In the subjects who underwent an acute Stanford A aortic dissection surgery, preoperative P_{aO_2}/F_{IO_2} ≤ 300 mm Hg, long cardiac arrest time, and massive blood transfusion (after surgery, >6 units in 24 h or >3,000 mL) were predictors of postoperative hypoxemia.[20,21] In the subjects after surgical aortic valve replacement, age, COPD, congestive heart failure, and bleeding disorders were associated with 30-d re-intubation.[22] Similarly, in subjects after thoracic surgery, American Society of Anesthesiology physical status classification of ≥ III, surgery duration > 80 min, fluid balance during operation > 4,000 mL were found to be independent risk factors of postoperative hypoxemia.[23-28] During abdominal surgery, including hepatectomy, upper or upper and lower (vs lower) abdominal incision, multiple procedures (vs one), crystalloid replacement > 6 L, and total surgery duration > 5 h were found to be risk factors.[29-31]

Efforts to predict the likelihood of postoperative pulmonary complications have been made. Canet et al[32] developed a scoring tool, the ARISCAT (assessed respiratory risk in surgical patients in Catalonia) score, to predict postoperative pulmonary complications based on their surgical cohort. Components of this score include age, preoperative S_{pO_2} and hemoglobin, previous respiratory infection within 1 month of surgery, surgical incision (abdominal or intrathoracic), surgery duration, and planned versus emergency status of the surgery; the risk level was considered as moderate with an ARISCAT score ≥ 26.[32] This scoring tool has been used in several randomized controlled trials (RCTs) that sought to better understand how to prevent or manage postoperative hypoxemia. To the best of our knowledge, a scoring tool specific for the prediction of postoperative hypoxemia has not yet been published.

Prophylactic Versus Curative Use of Respiratory Support for Postoperative Patients

Oxygen therapy has been recommended in the perioperative period to reduce surgical-site infections by the World Health Organization.[33] In postoperative patients, standard O_2 therapy, such as low-flow nasal cannula, a simple face mask, or an air-entrainment mask is routinely applied after extubation. In recent years, high-flow nasal cannula (HFNC) oxygen therapy has been increasingly used for postoperative patients after extubation. HFNC oxygen therapy provides a constant F_{IO_2} and generates some degree of PEEP and has been shown to improve oxygenation for patients who are hypoxemic.[34] The PEEP generated by HFNC is variable and depends on gas-flow settings, nasal cannula size, the patient's breathing pattern, and whether the mouth is open or closed.[35] In contrast, CPAP and noninvasive ventilation (NIV) provide constant positive airway pressure, which recruits alveoli or maintains alveolar recruitment. By providing 2 levels of positive pressure, NIV augments tidal volume and reduces the work of breathing. Importantly, both CPAP and NIV can be used for patients who tend to mouth breathe because they can be connected with an oronasal mask, total face mask, or helmet. An important consideration with regard to respiratory support devices is timing. Respiratory support can be given prophylactically as a way to prevent extubation failure or curatively when signs of respiratory compromise are apparent. In addition, respiratory support can be provided as a way to facilitate extubation in patients at high risk, such as those with COPD.

Prophylactic Use of HFNC Versus Standard O_2 Therapy Versus NIV or CPAP

The aim of the prophylactic use of respiratory support is to reduce pulmonary complications, prevent respiratory failure, and avoid re-intubation.[36] Ten RCTs assessed the effects of HFNC and standard O_2 therapy in preventing respiratory failure and re-intubation in the immediate postoperative period (Table 1).[37-46] Of the 10 RCTs, 5 were conducted in subjects after cardiac surgery,[37-41] and 4 were conducted in subjects after thoracic surgery.[42-45] Only one trial was completed in subjects after major thoracic and abdominal surgery.[46] In the most recent systematic review and meta-analysis, which included these 10 RCTs, HFNC was associated with significant reductions in re-intubation and escalation of respiratory support when compared with standard O_2 therapy.[7] These effects were noted in cardiothoracic subjects, and a post hoc subgroup analysis suggested that the subjects with high-risk

Table 1. Characteristics of Randomized Control Trials With Postextubation Preventive Use: HFNC vs Standard O_2 Therapy

Study, y	Surgery Type	Timing	Risk	Re-Intubation Rate	Proportion of Subjects Receiving Escalation Therapy
Parke et al,[37] 2013	Cardiac surgery	After extubation	NR	2/169 vs 2/171	47/169 vs 77/171
Corley et al,[38] 2015	Cardiac surgery	After extubation	BMI ≥ 30 kg/m^2	0/81 vs 2/74	3/81 vs 5/74
Zochios et al,[39] 2018	Elective cardiac surgery	After extubation	COPD, asthma, lower respiratory tract infection in the preceding 4 wk, BMI ≥ 35 kg/m2, current (within past 6 wk) heavy smokers (>10 pack-years)	1/51 vs 5/49	3/51 vs 10/49
Sahin et al,[40] 2018	Cardiopulmonary bypass	After extubation	BMI ≥30 kg/m^2	0/50 vs 4/50	6/50 vs 15/50
Tatsuishi et al,[41] 2020	Off pump coronary artery bypass graft surgery	After extubation	NR	NR	NR
Ansari et al,[42] 2016	Lung resection surgery	Immediately after arrival in PACU	NR	NR	NR
Brainard et al,[43] 2017	Thoracic surgery	After extubation	NR	NR	1/18 vs 2/26
Yu et al,[44] 2017	Thoracoscopic lobectomy	After extubation	ARISCAT risk score ≥ 26	0/56 vs 5/54	2/56 vs 14/54
Pennisi et al,[45] 2019	Thoracotomy lung resection	Within 30 min after extubation	NR	1/47 vs 1/48	2/47 vs 3/48
Futier et al,[46] 2016	Abdominal or abdominal and thoracic	After extubation	ARISCAT risk score ≥ 26	NR	20/108 vs 14/112

HFNC = high-flow nasal cannula
NR = not reported
BMI = body mass index
PACU = postoperative acute care unit
ARISCAT = assessed respiratory risk in surgical patients in Catalonia

Table 2. RCTs Comparing the Prophylactic Use of NIV or CPAP vs Standard O_2 Therapy Immediately Postextubation for Postoperative Subjects

Study, y	Comparison	Surgery Type	Timing	Re-Intubation Rate	Other Outcomes
Aguiló et al,[47] 1997	NIV vs standard O_2 therapy	Lung resection	Immediately after extubation	NR	NIV improved the efficiency of the lung without noticeable adverse effects
Joris et al,[48] 1997	NIV vs standard O_2 therapy	Gastroplasty	During the first 24 h after surgery	NR	NIV significantly reduced pulmonary dysfunction
Ebeo et al,[49] 2002	NIV vs standard O_2 therapy	Gastric surgery	First 24 h after surgery	NR	NIV improved recovery of pulmonary function
Perrin et al,[50] 2007	NIV vs standard O_2 therapy	Lung resection	7 d before surgery and 3 d after surgery	NR	NIV reduced pulmonary dysfunction, reduced hospital LOS
Carlsson et al,[51] 1981	CPAP vs standard O_2 therapy	Cholecystectomy	Admitted to the postoperative ward	NR	No difference on any physiologic variable
Lindner et al,[52] 1987	CPAP vs standard O_2 therapy	Elective upper abdominal surgery	1 h after extubation	NR	CPAP improved postoperative pulmonary function recovery
Pinilla et al,[53] 1990	CPAP vs standard O_2 therapy	CABG	Immediately after extubation, for 12 h	NR	Initial P_{aO_2} increased with CPAP
Thomas et al,[54] 1992	CPAP vs standard O_2 therapy	CABG	Immediately after extubation, for 1 h	NR	Oxygenation improved with CPAP
Jousela et al,[55] 1994	CPAP vs standard O_2 therapy	CABG	Immediately after extubation, for 8 h	NR	Initial oxygenation improved with CPAP
Böhner et al,[56] 2002	CPAP vs standard O_2 therapy	Major vascular surgery	Admission to the ICU	1/99 (1%) vs 5/105 (5%); $P = .21$	Severe oxygenation problems reduced with CPAP
Gaszynski et al,[57] 2007	CPAP vs standard O_2 therapy	Open Roux-en-Y gastric bypass	Admission to the PACU	NR	Oxygenation improved with CPAP
Neligan et al,[58] 2009	CPAP vs standard O_2 therapy	Laparoscopic bariatric surgery	Immediately after extubation	NR	Pulmonary function recovered faster with CPAP
Kindgen-Milles et al,[59] 2005	Continuous CPAP vs intermittent CPAP	Thoracoabdominal aortic surgery	Immediately after extubation	1/25 (4%) vs 4/25 (16%); $P = .02$	Continuous CPAP had fewer pulmonary complications, and shorter hospital LOS
Zarbock et al,[60] 2009	Continuous CPAP vs intermittent CPAP	Cardiac surgery	Immediately after extubation	3/232 (1%) vs 6/236 (3%); $P = .030$	Continuous CPAP improved oxygenation, decreased pulmonary complications and ICU readmission
Stock et al,[61] 1985	CPAP vs IS vs cough and deep breath	Upper abdominal operation	After extubation	NR	No differences in outcomes
Ricksten et al,[62] 1986	CPAP vs PEP vs IS	Upper abdominal surgery	After extubation	NR	Oxygenation improved with CPAP and PEP; FVC was higher with CPAP and PEP; the incidence of atelectasis was lower with CPAP and PEP

(Continued)

Table 2. Continued

Study, y	Comparison	Surgery Type	Timing	Re-Intubation Rate	Other Outcomes
Denehy et al,[63] 2001	CPAP 30 mins per session, 4 sessions per day for 3 days vs CPAP 15 mins per session, 4 sessions per day for 3 days	Upper abdominal surgery	First day after operation	NR	No difference in PFT results or oxygenation
Fagevik Olsén et al,[64] 2002	CPAP vs breathing exercises by inspiratory resistance–positive expiratory pressure	Thoracoabdominal resection	Immediately after extubation	7/36 (19%) vs 1/34 (3%), $P = .030$	Mechanical ventilation duration was shorter with CPAP
Matte et al,[65] 2000	NIV vs CPAP vs IS	CABG	Immediately after extubation	NR	NIV and CPAP improved pulmonary function and P_{aO_2}
Pasquina et al,[66] 2004	NIV vs CPAP	Cardiac surgery	Immediately after extubation	1/75 (1%) vs 1/75 (1%)	Atelectasis score improved more with NIV

RCT = randomized, controlled trial
NIV = noninvasive ventilation
NR = not reported
CABG = coronary artery bypass grafting
PACU = postoperative acute care unit
LOS = length of stay
IS = incentive spirometry
PEP = positive expiratory pressure
PFT = pulmonary function test

factors such as BMI ≥ 30 kg/m^2, ARISCAT score ≥ 26, or chronic pulmonary disease benefited the most from HFNC.[7] There were no significant effects on other important clinical outcomes, such as mortality, ICU length of stay, and hospital length of stay. The prophylactic use of HFNC was recommended in patients with high-risk factors after cardiothoracic surgery (Fig. 1). When considering that the only RCT of the subjects who underwent abdominal surgery did not find any significant differences between HFNC and standard O_2 therapy;[46] currently, no recommendation is made for patients after abdominal surgery.

Similarly, multiple RCTs compared the prophylactic use of NIV or CPAP versus standard O_2 therapy for postoperative subjects (Table 2), but all were completed before 2009 and most were the comparison of CPAP versus standard O_2 therapy.[47-66] Of the 20 RCTs, only 5 reported re-intubation rates,[56,59,60,64,66] in which one compared CPAP and standard O_2 therapy.[56] In the CPAP versus standard O_2 therapy study, no significant differences in re-intubation rates were found. In the remaining 4 studies,[59,60,64,66] 2 studies compared the continuous versus intermittent use of CPAP and found lower re-intubation rates with continuous CPAP;[59,60] however, the clinical implication of this finding was questionable due to the concerns of patient comfort and complications of continuous CPAP, for example, skin breakdown. In addition, the low incidence of re-intubation rates in those subjects is also of concern. In the study reported by Zarbock et al,[60] the re-intubation rates were reduced from 2.5% to 1.3% by using continuous CPAP, which might not be clinically meaningful.

Stéphan et al[67] conducted a unique RCT to compare HFNC with NIV for subjects after cardiothoracic surgery, who were divided into 3 groups: 1) subjects who passed a spontaneous breathing trial (SBT) and had one of 3 high-risk factors (BMI > 30 kg/m^2, left-ventricular ejection fraction of <40%, or failure of previous extubation); 2) subjects who passed an SBT but developed hypoxemic respiratory failure after extubation; 3) subjects in whom an SBT failed but were still extubated. Randomization was stratified based on the 3 groups. Interestingly, even though the outcomes between the 2 overall groups were not significantly different, the subgroup analysis on the prophylactic use of HFNC versus NIV for the subjects with high-risk factors showed lower rates of treatment failure in the HFNC group (5.7% vs 12.6%; P =.04).[67] This result might be explained by the better compliance and longer use of HFNC than NIV due to patient comfort and convenience with the 2 devices. This is the only RCT that compared the prophylactic use of HFNC with NIV for subjects after surgery. Future RCTs with larger sample size are needed to confirm this finding.

Curative Use of NIV or CPAP Versus Standard O_2 Therapy Versus HFNC

In a recently published European Society of Anaesthesiology and European Society of Intensive Care Medicine guideline,[68] compared with standard O_2 therapy, NIV or CPAP is recommended to treat patients with perioperative or periprocedural hypoxemia to improve oxygenation. So far, 8 RCTs compared the use of NIV or CPAP and standard O_2 therapy in subjects after surgery who had already developed hypoxemic respiratory failure (Table 3).[69-76] Of the 8 studies, 5 were completed in subjects after cardiothoracic surgery[70-72,74,76] and 3 were completed in subjects who underwent abdominal surgery.[69,73,75] NIV was used in 6 RCTs and significantly reduced the re-intubation rates in the subjects after cardiothoracic or abdominal surgery.[69-74] Interestingly, Yang et al[74] compared the use of NIV with a helmet versus an oronasal mask versus standard O_2 therapy in their subjects after Stanford type-A aortic dissection; only NIV with the helmet was found to significantly reduce re-intubation rates compared to standard O_2 therapy. Conversely, no significant difference was found between the groups that used NIV with oronasal mask and standard O_2 therapy. The superiority of the helmet over the oronasal mask agrees with the findings by Patel et al[77] that the lower intubation rate was found in the group of subjects with acute hypoxemia and receiving NIV via the helmet than those receiving NIV via the oronasal mask. However, its benefits in postoperative patients with hypoxemic respiratory failure still need future studies with larger sample sizes to confirm.

Only 2 RCTs compared CPAP with standard O_2 therapy.[75,76] No significant differences were found in the re-intubation rates of subjects after cardiac surgery, with a P_{aO_2}/F_{IO_2} of 100–250 mm Hg.[76] In contrast, Squadrone et al[75] found a lower re-intubation rate with CPAP compared with standard O_2 therapy in 209 subjects who developed hypoxemia within 1 h after abdominal surgery. Using CPAP in patients who have undergone gastrointestinal surgery should be done cautiously due to the concerns of anastomotic leakage caused by gas aspiration. The findings from the 2 RCTs might suggest that CPAP is most effective as a preventive strategy rather than a therapeutic modality.[75,76] It seems that, for patients who develop hypoxemic respiratory failure after cardiothoracic or abdominal surgery, NIV reduces re-intubation rates compared with standard O_2 therapy (Fig. 1) and NIV with the helmet might be more beneficial than an oronasal mask. The early use of CPAP might be helpful but only in patients after abdominal surgery.

To our knowledge, no study has been done to compare the use of HFNC and standard O_2 therapy to treat postoperative patients with hypoxemic respiratory failure. As reported in the aforementioned section, one of the 3 subgroups in the RCT by Stéphan et al[67] compared the curative

Table 3. RCTs Compared the Curative Use of NIV or CPAP and Standard O_2 Therapy in Postoperative Subjects Who Developed Hypoxemic ARF

Study, year	Comparison	Surgery Type	Timing	Re-Intubation Rate	Other Outcomes
Antonelli et al,[69] 2000	NIV vs standard O_2 therapy	Solid organ transplantation	Developed hypoxemic ARF after surgery	4/20 (20%) vs 14/20 (70%); $P = .002$	Shorter ICU LOS, lower ICU mortality with NIV
Auriant et al,[70] 2001	NIV vs standard O_2 therapy	Lung resection	Postoperative development of hypoxemic ARF	5/24 (21%) vs 12/24 (50%); $P = .035$	Lower mortality with NIV
Michelet et al,[71] 2009	NIV vs standard O_2 therapy	Esophagectomy	Developed ARF	9/36 (25%) vs 23/36 (64%); $P = .008$	Lower ARDS rate, ICU LOS, and less anastomotic leakage with NIV
Zhu etal,[72] 2013	NIV vs standard O_2 therapy	Cardiac surgery	$P_{aO_2} \leq 60$ mm Hg; $P_{aO_2}/F_{IO_2} \leq 200$ mm Hg	9/48 (19%) vs 38/47 (81%); $P < .001$	Lower tracheostomy rate, VAP incidence, in-hospital mortality, and shorter duration of ventilation and ICU LOS in the NIV group
Jaber et al,[73] 2016	NIV vs standard O_2 therapy	Abdominal surgery	Hypoxemic ARF within 7 d of surgery	49/148 (33%) vs 66/145 (46%); $P = .030$	Fewer re-intubations, less VFD, fewer infections with NIV
Yang et al,[74] 2016	NIV (mask) vs NIV (helmet) vs standard O_2 therapy	Stanford type A aortic dissection	Hypoxemia within 24 h after extubation	8/25 (32%) vs 2/25 (8%) vs 9/25 (36%); $P = .048$	NIV (helmet) may quickly improve P_{aO_2}, decrease P_{aCO_2}, and shorter hospital LOS
Squadrone et al,[75] 2005	CPAP vs standard O_2 therapy	Abdominal surgery	Hypoxemia within 1 h after abdominal surgery	1/105 (1%) vs 10/104 (10%); $P = .005$	Lower incidence of pneumonia; infection, and sepsis with CPAP
Olper et al,[76] 2017	CPAP vs standard O_2 therapy	Cardiac surgery	P_{aO_2}/F_{IO_2} 100–250 mm Hg	0/33 (0%) vs 1/31 (3%); $P = .48$	CPAP was associated with a significant reduction in the number of subjects with $P_{aO_2}/F_{IO_2} < 200$ mm Hg (4/33 [12%] vs 14/31 [45%]; $P = .003$)

RCT = randomized controlled trial
NIV = noninvasive ventilation
ARF = acute respiratory failure
LOS = length of stay
VAP = ventilator-associated pneumonia
VFD = ventilator-free day

use of HFNC and NIV for subjects after cardiothoracic surgery in whom extubation failed, no significant differences of treatment failure rates were found between HFNC and NIV (27.4% vs 27.8%; $P = .93$). This suggests that HFNC might be considered as an alternative to NIV to treat hypoxemic respiratory failure in patients who undergo cardiothoracic surgery, especially for those who do not tolerate NIV.

Facilitative Extubation With NIV Versus HFNC

Patients in whom traditional weaning attempts fail usually continue invasive ventilation until passing an SBT. However, the risks of continuing invasive ventilation are significant for some patients, such as those that are immunocompromised.[68] Thus, early extubation for those patients might play an important role in their outcomes.[36] The European Respiratory Society and American Thoracic Society guideline[78] suggests using NIV to facilitate weaning from invasive ventilation in patients with hypercapnic respiratory failure, whereas no recommendation was provided for patients who are hypoxemic. Recently, Vaschetto et al[79] conducted an RCT in a group of highly selected subjects who were hypoxemic and found that early extubation followed by immediate NIV application reduced the days on invasive ventilation without affecting the length of ICU stay.

Similarly, in a historical comparison study implemented by Liu et al,[80] early extubation followed by subsequent NIV significantly reduced the duration of invasive ventilation and the length of ICU stay in postoperative subjects in whom the first SBT failed. A small subgroup of postoperative subjects in the Stéphan et al[67] RCT were evaluated on the effects of NIV versus HFNC to facilitate weaning in postoperative patients. A trend toward higher treatment failure was found in patients who were extubated to HFNC versus those who were treated with NIV (40.7% vs 28.0%; $P = .33$). The evidence supporting early extubation to NIV after surgery is still lacking. The use of NIV to facilitate early extubation for postoperative patients in whom an SBT failed should be done so with caution.

Optimize Respiratory Support

Appropriate settings to achieve optimal treatment effects are essential for treatment success when respiratory support is used. For patients who developed atelectasis after cardiac surgery, Pasquina et al[66] compared the use of NIV and CPAP in an RCT, and found that more subjects in the NIV group had radiologic improvement of atelectasis (60% vs 40%; $P = .02$). This finding supports the use of inspiratory pressure provided by NIV rather than a constant positive pressure that does not change between the phases of the breath. More importantly, the key to NIV success seems to be sufficient driving pressure. Joris et al[48] compared the inspiratory and expiratory positive pressure settings of 12 and 4 cm H_2O, respectively, with pressure settings of 8 and 4 cm H_2O, and no NIV in subjects with obesity who underwent gastroplasty. They found only the subjects in the NIV settings of 12 and 4 cm H_2O had significant improvement in pulmonary function after surgery, whereas no significant differences were found in the groups of NIV setting at 8 and 4 cm H_2O and no NIV.[48] For the utilization of HFNC, flow settings play a key role in treatment success. However, no consensus has been achieved in the flow settings for patients with different etiologies and situations. Particularly, the individual patient's inspiratory flow may vary breath by breath. One universal setting does not fit all; an individualized setting and timely adjustment should be considered.

Clinical Monitoring During Respiratory Support

Close monitoring is necessary to ensure the success of respiratory support, particularly the first 1 h of initiating treatment because most patients who improve with treatment will do so within the first hour. Although delaying intubation is associated with increased mortality, escalation of therapy is warranted if the patients do not respond to treatment in the first hour.[81] Common monitoring variables include breathing frequency, accessory muscle use, or work of breathing, S_{pO_2}, and P_{aO_2}/F_{IO_2}.[11] More recently, the ROX index, defined as the ratio of S_{pO_2}/F_{IO_2} to frequency, has been described and prospectively validated to predict the failure of HFNC in patients with acute respiratory failure caused by pneumonia, and the cutoff value was determined as 4.88.[82-84] However, the sensitivity and specificity of the ROX index in patients who were hypoxemic after surgery and the threshold to determine HFNC failure require further investigation.

When NIV is used, special attention should be paid to risk factors for NIV failure, such as copious secretions with ineffective cough ability, hemodynamic instability, and the intolerance to the interface or positive pressure. Duan et al[85] developed the HACOR score (heart rate, acidosis, consciousness, oxygenation, and respiratory rate) to predict NIV failure among patients who are hypoxemic. The scale seemed effective in predicting NIV failure in a separate cohort of subjects with hypoxemia. An HACOR score > 5 after 1 h use of NIV was a cutoff point to determine NIV failure, and intubation was recommended.

Making the determination of treatment failure and knowing when to escalate therapy, such as endotracheal intubation and mechanical ventilation, are challenging. We summarized the intubation criteria from all the RCTs by comparing HFNC and NIV or CPAP versus standard O_2 therapy in Table 4. The most common criteria are 1) tachypnea with a frequency > 35 breaths/min and accessory muscle use; 2) respiratory acidosis, with $pH < 7.30$

Table 4. Intubation Criteria Used in the RCTs that Compared HFNC, CPAP, NIV vs Standard O_2 Therapy

Parameter	HFNC vs Standard O_2 Therapy	NIV or CPAP vs Standard O_2 Therapy
Breathing frequency	25–35 breaths/min; bradypnea or respiratory arrest	>35 breaths/min; ≥20% increase in frequency
Respiratory acidosis	pH < 7.30 and $P_{aCO_2} \geq 50$ mm Hg	pH < 7.30 and $P_{aCO_2} \geq 50$ mm Hg
Breathing pattern	Accessory muscle use; paradoxical abdominal or thoracic motion; clinical signs of muscle fatigue	Accessory muscle use; paradoxical abdominal or thoracic motion
Refractory/severe hypoxemia	$S_{pO_2} < 88\%$ with F_{IO_2} 1.0; $S_{pO_2} < 90\%$ with $F_{IO_2} \geq 0.5$ or $P_{aO_2}/F_{IO_2} < 200$ mm Hg; $S_{pO_2} < 92\%$ while breathing at least 10 L/min oxygen, $P_{aO_2} < 60$ mm Hg on air or $P_{aO_2} < 80$ mm Hg while breathing O_2	$P_{aO_2} < 45$ mm Hg despite oxygen supplementation;$P_{aO_2} < 45$ mm Hg combined with a failure to increase F_{IO_2} or $P_{aO_2}/F_{IO_2} <$ 140 mm Hg; a decrease in P_{aO_2} compared with the respective values at the study outset; failure to maintain a $P_{aO_2} > 65$ mm Hg with an $F_{IO_2} \geq 0.6$; $S_{pO_2} < 80\%$, despite the use of the maximum F_{IO_2}; ≥20% increase in P_{aCO_2}
Mental status	Encephalopathy; altered state of consciousness; clinical findings of exhaustion	Loss of consciousness; occurrence of seizures or coma (Glasgow scale < 8); severe agitation
Hemodynamic status	Unstable; increased mean arterial blood pressure	Cardiac arrest; heart rate of <50 beats/min with loss of alertness; severe hemodynamic instability without response to fluid and vasoactive drugs; hemodynamic instability defined as: 1) an 80- to 90-mm Hg increase or a 30- to 40-mm Hg decrease in SBP from to the baseline, 2) the need for inotropic drugs for at least 2 h to maintain SBP > 85 mm Hg, 3) electrocardiogram evidence of ischemia or significant ventricular arrhythmias
Airway protection	NR	Weak cough reflex with secretion accumulation; development of conditions that necessitate endotracheal intubation to protect the airways (coma or seizure disorders) or to manage copious tracheal secretions

RCT = randomized controlled trial
HFNC = high-flow nasal cannula
NIV = noninvasive ventilation
NR = not reported
SBP = systolic blood pressure

and $P_{aCO_2} > 50$ mm Hg; 3) altered mental status; 4) hemodynamic instability; and 5) loss of the ability to protect the airway. The only controversial criterion is for refractory hypoxemia, which varies greatly in RCTs.

Other Treatments

Incentive Spirometry

Incentive spirometry (IS) encourages patients to perform deep breathing exercises independently, with visual feedback of inspiratory effort.[86] Since the introduction in 1970, IS has been broadly used for postoperative patients to prevent and treat pulmonary complications, such as atelectasis or pneumonia.[87,88] However, data with regard to its effectiveness are conflicting, and high-quality evidence is lacking.[89] In a recently published systematic review and meta-analysis of 95 RCTs, no significant differences in patient outcomes were found between IS and standard medical care (risk ratio 1.06, 95% CI 0.85–1.34).[90] However, in the RCT of subjects after coronary artery bypass grafting, Eltorai et al[91] found that the use of IS significantly improved the radiographic atelectasis severity score, the need for NIV, length of stay in the ICU and hospital, and 6-month mortality in a subgroup of subjects after non-elective surgery. Importantly, in this study, a reminder bell was used in the experimental group. This increased adherence to IS when compared with the control group, which had no reminder bell. [91] This finding suggests that using IS correctly may be the key to treatment success. In a large national survey of health-care providers, respondents reported that patients might forget to use their incentive spirometer, which contributed to therapy nonadherence.[92] To accurately assess and harness the true value of IS for postoperative patients, efforts aimed at improving IS adherence are warranted.[93]

Inhaled Pulmonary Vasodilators

Inhaled pulmonary vasodilators have been increasingly used to improve oxygenation for patients with hypoxemia by correcting a ventilation/perfusion mismatch.[94] They are also used in patients with hypoxemia and with pulmonary hypertension and/or right heart failure to reduce pulmonary arterial pressure. Small cohort studies demonstrated that inhaled pulmonary vasodilators via HFNC or NIV can reduce pulmonary arterial pressure and/or improve oxygenation in patients after cardiac surgery,[95-99] but larger RCTs are needed to validate these findings.[100] Inhaled pulmonary vasodilators can improve hypoxemia but did not reverse the underlying condition.

Non-Opioid Analgesics

Adverse events due to respiratory depression often occur on the first postoperative day due to the administration of opioids.[101] Non-opioid analgesics have been proposed as a way to control pain while reducing the use of opioids. This would, at least in theory, reduce the incidence of postoperative hypoxemia.[101] However, in a recent double-blind RCT with 570 subjects after abdominal surgery, no significant difference in the duration of postoperative hypoxemia was found between the groups of subjects treated with opioids and with non-opioids.[102] Future studies are needed to investigate the role of non-opioid analgesics in postoperative hypoxemia.

Areas of Uncertainty and Future Research

Some uncertainties remain in the prevention and management of postoperative hypoxemia. A comprehensive scoring system that uses risk factors specific for postoperative hypoxemia is needed to determine patients at high risk. For those postoperative patients who are considered high risk, the prophylactic use of HFNC versus NIV needs to be determined. The role of HFNC for patients after abdominal surgery compared with standard O_2 therapy needs further investigation. For patients for whom a planned extubation failed, whether HFNC or NIV is more effective to prevent re-intubation is still unknown. NIV has theoretic superiority over CPAP for reducing work of breathing and prevention of atelectasis in postoperative patients, but whether this translates to better clinical outcomes is still unclear. The combination of HFNC and NIV, meaning the utilization of HFNC during NIV breaks, has shown to be more effective than NIV alone in reducing re-intubation in nonsurgical patients at high risk.[103] Whether this combination has similar benefits in patients after surgery and with high-risk factors warrants further study. Also, whether the combined use of oxygen therapy with adjunct therapy, for example, lung expansion therapy and inhaled pulmonary vasodilators, would generate better outcomes for patients after surgery is unknown.

Summary

Postoperative hypoxemia is common in clinical practice. Compared with patients without postoperative hypoxemia, these patients have longer lengths of stay and higher mortality in an ICU and hospital. Special attention needs to be paid to patients with risk factors, specifically age $>$ 65 years, BMI $\geq$ 30 kg/m^2, American Society of Anesthesiology physical status classification $\geq$ III, ARISCAT score $\geq$ 26, preoperative dependent living status, preoperative sepsis, or chronic pulmonary disease such as moderate-to-severe COPD, asthma, or obstructive sleep apnea. Analysis of the currently available evidence suggests that the prophylactic use of HFNC benefits patients at high risk of hypoxemic respiratory failure after cardiothoracic surgery. For patients in whom planned extubation failed after surgery, NIV should be used to treat hypoxemic respiratory failure and to avoid re-intubation, whereas early CPAP should only be considered for patients after abdominal surgery. If a patient is intolerant of NIV or CPAP, HFNC might be considered as an alternative. Close monitoring of the patient's response to treatment within the first hour of initiation is essential in treatment success and escalation of therapy should be considered when no improvement is observed.

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