

Noninvasive Respiratory Support for Postextubation Respiratory Failure

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Summary

The rate of re-intubation after endotracheal extubation for all indications is estimated at ~20%. This high rate is related, in part, to the development of postoperative complications that leads to acute respiratory failure that requires re-intubation. In general, 5–10% of all surgical patients develop postoperative respiratory failure, and, in patients who require abdominal surgery, up to 40% develop respiratory failure. The forms of respiratory support that have been shown to be most effective in managing postextubation respiratory failure and preventing re-intubation are noninvasive ventilation, CPAP, and high-flow nasal cannula. From an analysis of the data, it is clear that patients at high risk of re-intubation require CPAP, noninvasive ventilation, or high-flow nasal cannula after extubation to allow for a smooth transition to spontaneous breathing and to minimize the need for re-intubation. CPAP is most indicated in patients with atelectasis in which high levels of PEEP are needed, noninvasive ventilation is indicated in the patient unable to maintain an adequate minute ventilation without excessive work of breathing, and high-flow nasal cannula is indicated in the patient with severe hypoxemia that was not a result of marked atelectasis or severe ARDS. It is also clear that there are insufficient data to support the use of any of these therapies in patients at low risk for re-intubation or the development of postoperative pulmonary complications. *Key words:* CPAP; noninvasive ventilation; high-flow nasal cannula; re-intubation; acute respiratory failure; postoperative pulmonary complications. [Respir Care 2019;64(6):658–678. © 2019 Daedalus Enterprises]

Introduction

The rate of re-intubation after endotracheal extubation for all indications is estimated at ~20%.^{1,2} This high rate is related, in part, to the development of postoperative complications that leads to acute respiratory failure (ARF) that requires re-intubation.³⁻⁵ Atelectasis, pneumonia, bronchospasm, and pulmonary embolism as well as a myriad of systemic problems can lead to respiratory failure.⁶⁻⁸ In addition, nonsurgical subjects with comorbidities, COPD, heart disease, obesity (body mass index > 35 kg/m²), age (>65 years), multiple weaning failures, increased sputum production, and upper-airway obstruction also have an increased likelihood of developing postextubation respiratory failure that requires re-intubation.^{9,10}

In general, 5–10% of all surgical patients develop postoperative respiratory failure, and, in patients who require abdominal surgery, up to 40% develop respiratory failure.^{11,12} Particularly in patients undergoing abdominal surgery, postoperative respiratory muscle dysfunction is common.¹³ Thoracic, abdominal, and diaphragmatic muscles can be compromised as well as the phrenic nerve being dysfunctional.¹⁴ All of this increases the likelihood of development of postoperative ARF. The forms of postextubation respiratory support that have been shown to be most effective in managing postextubation respiratory failure and preventing re-intubation are noninvasive ventilation (NIV), CPAP, and high-flow nasal cannula (HFNC). This review focused on comparing and contrasting these forms of respiratory support in adults after extubation and in identifying the circumstances in which each form of therapy is most indicated.

Types of Respiratory Support

NIV

NIV results in the same physiologic effects as invasive ventilation. With a properly fitting oronasal mask, ventilation and oxygenation can be titrated to the patient's ven-

Table 1. Benefits of High-Flow Nasal Cannula

| Benefit |
|---|
| Precise, consistent, high concentration of oxygen |
| Upper airway dead space reduced by 33% |
| Reduced work of breathing |
| Reduced minute ventilation |
| Low-level CPAP |
| Improved comfort vs NIV or CPAP |
| Improved tolerance vs NIV or CPAP |

NIV = noninvasive ventilation

tilatory demand similar to that with invasive ventilation. However, NIV has to be applied by oronasal mask or a similar type of interface. As a result, the primary concern with NIV is patient intolerance due to discomfort.¹⁵ Pressure ulcers, drying of oral and/or pharyngeal secretions, sinus and ear pain, eye irritation, and gastric distention are common adverse effects, whereas aspiration, pneumothorax, and hypotension are infrequent adverse effects.¹⁵

CPAP

CPAP is the application of PEEP to the patient who is spontaneously breathing and not on mechanical ventilation. As with invasive application of CPAP, a consistent level of PEEP can be applied in levels up to and exceeding 20 cm H₂O. Analysis of recent data indicates that the neural respiratory drive and breathing effort assessed by electrical activity of the diaphragm is similar with nasal CPAP and HFNC.¹⁶ As with NIV, patient tolerance of mask application and discomfort are primary problems with CPAP.¹⁵ Adverse effects associated with CPAP are also the same as with NIV.¹⁵

HFNC

HFNC is the application of a high flow of oxygen through a specially designed cannula. The proposed benefits of HFNC are a precise, consistent, and high concentration of delivered oxygen;^{17,18} wash out of CO₂ from the upper airway, which reduces dead space ventilation by ~33% and results in reduced minute ventilation¹⁹⁻²² and work of breathing;²³ and the establishment of a low level of CPAP (Table 1).²⁴⁻²⁷ However, the CPAP established is based on numerous variables, including gas flow, leak volume, fitting of the cannula into a patient's nares, and the size of the patient.²¹ Importantly, because HFNC is administered at approximate body temperature and saturated with water vapor, it is usually well tolerated by patients in all age groups. Most of the adverse effects observed with NIV and CPAP have not been reported with HFNC. Secretion is-

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sues as a result of inadequate humidification and pressure ulcers on the top of the ears as a result of the cannula straps and around the nares are the most common adverse effects.²¹

NIV Postextubation in the ICU for ARF

A number of randomized controlled trials (RCTs) were performed to evaluate NIV postextubation in the ICU for ARF. In most of these studies, the majority of the subjects had a history of COPD (Table 2).

NIV Postextubation After a Failed Spontaneous Breathing Trial

The use of NIV as a support and transition mode to unsupported spontaneous breathing in patients with COPD for whom a spontaneous breathing trial (SBT) failed was evaluated in 5 RCTs.^{10,28-31} After 48 h of invasive ventilation and a failed SBT, Nava et al²⁸ randomized subjects with COPD to either pressure support ventilation (PSV) or extubation to NIV. A total of 50 subjects were randomized, 25 to each group. At 60 d, 68% of the subjects in the PSV group were weaned, and 88% of the subjects who received NIV were weaned. The mean duration of mechanical ventilation was longer in the PSV group versus the NIV group ($P = .02$), 16.6 ± 11.8 d versus 10.2 ± 6.8 d. For patients receiving NIV, the probability of survival and weaning was higher ($P = 0.002$) and time in the ICU was shorter (mean \pm SD, 15.1 ± 5.4 d versus 24.0 ± 13.7 d for patients who received invasive ventilation; $P = 0.005$). At 60 d, 92% of the subjects in the NIV group survived and 72% of the subjects in the PSV group survived, $P = .009$. Girault et al²⁹ studied 33 subjects with COPD for whom an SBT also failed. As with Nava et al,²⁸ the subjects were randomized to remain intubated while receiving PSV ($n = 16$) or to be extubated to NIV ($n = 17$). In the NIV group, 13 of 17 were weaned, and 12 of 16 in the PSV group were weaned, $P > .05$. The duration of invasive ventilation was shorter, as expected with NIV (mean \pm SD, 4.56 ± 1.85 d versus 7.69 ± 3.79 d, $P = .004$). NIV reduced the total duration of ventilatory support but increased the time devoted to weaning (mean \pm SD, 3.46 ± 1.42 d versus 11.54 ± 5.24 d, $P = <.001$). At 3 months, the length of ICU and hospital stays were similar. No differences in mortality were reported.

The third study in this group, by Ferrer et al,¹⁰ had a slightly different protocol; the subjects had to fail SBTs on 3 consecutive days, and only ~50% of the 43 subjects randomized had COPD. The NIV group versus the PSV group had fewer days of mechanical ventilation (mean \pm SD, 9.5 ± 8.3 d versus 20.1 ± 13.1 d, $P = .003$), fewer ICU days (mean \pm SD, 14.1 ± 9.2 d versus 25.0 ± 12.5 d, $P = .002$), fewer hospital days (mean \pm SD, 27.8 ± 14.6 d

versus 40.8 ± 21.4 d, $P = .03$), and greater ICU survival (90% versus 56%, $P = .045$). Trevisan et al³⁰ randomized subjects who required mechanical ventilation > 48 h and failing a T-piece trial to NIV ($n = 28$) or continued invasive ventilation ($n = 37$). In both groups, ventilation times to T-piece trial were the same, 7.3 ± 4.1 d. There were no differences in the re-intubation rate, length of stay (LOS) in the ICU, or mortality. However, the NIV group had a lower pneumonia rate and lower need for tracheotomy.

The final RCT in this group was a second study by Girault et al.³¹ They randomized 208 subjects with COPD in whom their first SBT failed to 3 groups: continued invasive ventilation ($n = 69$), extubation to oxygen therapy ($n = 70$), and extubation to NIV ($n = 69$). Re-intubation rates did not differ with 30% of the subjects with invasive ventilation, 37% subjects of oxygen therapy, and 32% of subjects on NIV ($P = .65$). Weaning failure rates, including postextubation ARFs, were lower in the NIV group (54% invasive ventilation, 71% oxygen therapy, and 33% NIV; $P < .001$). Weaning time was longer in the NIV group than in the invasive ventilation group, 2.5 versus 1.5 d, $P = .033$.

Although taken as a group, there is clear support for extubating patients with COPD after a failed SBT and managing them with NIV, this has not become a widespread routine standard of care. There is that underlying fear that patients who failed an SBT will fail extubation and require re-intubation. Yes, we do extubate these patients to NIV but only under select circumstances. Specifically, we extubate a patient who is slated for tracheostomy when the clinical team considers them weanable but the patient continually fails SBTs, and any patient for whom analysis of all of the data indicates that the patient should be able to wean from ventilatory support but keeps failing SBTs.

Passed an SBT but High Risk for Re-Intubation

NIV has proven to be the most effective postextubation modality in patients in the ICU who passed an SBT but are considered high risk for re-intubation. High risk has been defined as a history of COPD or congestive heart failure, multiple attempts at weaning before SBT success, APACHE (Acute Physiology and Chronic Health Evaluation) II > 12 on the day of extubation, upper-airway obstruction, > 65 years old, ineffective cough, or excessive airway secretions.³²⁻³⁵ Four RCTs address this issue. Nava et al³² randomized 97 subjects who required > 48 h of mechanical ventilation who passed an SBT and demonstrated one of the factors associated with high risk of extubation failure to NIV or to standard oxygen therapy after extubation. NIV was provided at least 8 h per day for 48 h. The subjects who received NIV had a lower re-intubation rate (4 versus 12, $P = .03$). However, mortality (12% versus

Table 2. Postextubation ICU to NIV: Primarily Subjects With COPD

| Study, y | Study Design | Control | Subjects, n | Outcome |
|---|--|--|--|---|
| Failing Spontaneous Breath Trial | | | | |
| Nava et al. ²⁸ 1998 | RCT: >48 h invasive ventilation and failed SBT; PSV intubated vs extubation to NIV | PSV intubated | 25 in each group | At 60 d, more weaned NIV; 60 d survival greater NIV; NIV shorter ICU time, shorter ventilator time |
| Girault et al. ²⁹ 1998 | RCT: failed SBT; extubation to NIV vs PSV intubated | PSV intubated | 17 NIV, 16 PSV | Number weaned no difference; duration of mechanical ventilation, shorter with NIV; ICU and hospital LOS and mortality similar |
| Ferrer et al. ¹⁰ 2003 | RCT: failed SBT, 3 consecutive days; 50% of subjects did not have COPD; extubated to NIV vs PSV intubated | PSV intubated | 22 NIV, 21 PSV | NIV fewer ICU and hospital days greater ICU survival |
| Trevison et al. ³⁰ 2008 | RCT: >48 h invasive ventilation and failed SBT; extubated to NIV vs intubated for invasive ventilation | Invasive ventilation | 28 NIV, 37 invasive ventilation | No difference in intubation rate, ICU stay, or mortality; NIV lower rate of pneumonia and need for tracheostomy |
| Girault et al. ³¹ 2011 | RCT: failed the first SBT; 3 groups (continued invasive ventilation, extubated to O ₂ , extubated to NIV) | PSV intubated; extubated to O ₂ | 69 intubated, 70 O ₂ , 69 NIV | Re-intubation rate did not differ; weaning failure rate lower NIV; weaning time longer NIV |
| Passed SBT but high risk for re-intubation | | | | |
| Nava et al. ³⁴ 2005 | RCT: >48 h ventilation and passed SBT; all high risk for re-intubation; COPD, CHF, or APACHE II > 12 d of extubation; upper-airway obstruction; > 65 y old; ineffective cough or excessive secretion | O ₂ therapy | 48 NIV, 47 O ₂ | NIV lower re-intubation, hospital LOS, ICU LOS, and mortality |
| Ferrer et al. ³³ 2006 | RCT: >48 h ventilation and passed SBT; all high risk of re-intubation, COPD, CHF, or APACHE II > 12 d of extubation, upper-airway obstruction, > 65 y old, ineffective cough, or excessive secretion | O ₂ therapy | 79 NIV, 83 O ₂ | Less development of ARF with NIV, ICU mortality lower NIV, hospital mortality no difference |
| Ferrer et al. ³⁴ 2009 | RCT: >48 h ventilation and passed SBT; all high risk of re-intubation, COPD, CHF, or APACHE II > 12 d of extubation, upper-airway obstruction; > 65 y old; ineffective cough or excessive secretion; all the subjects had COPD | O ₂ therapy | 52 NIV, 54 O ₂ | Less development of ARF with NIV; 90-d mortality was lower with NIV |
| Khilnani et al. ³⁵ 2010 | RCT: Patients with severe COPD passed SBT; extubated to NIV vs O ₂ | O ₂ therapy | 20 NIV, 20 O ₂ | No difference in re-intubation, ICU LOS, or hospital LOS |
| NIV for extubation failure, developing ARF | | | | |
| Keenan et al. ³⁹ 2002 | RCT: passed SBT and within 48 h developed ARF; NIV vs O ₂ therapy | O ₂ therapy | 41 NIV, 40 O ₂ | No difference in re-intubation, ICU and hospital LOS and mortality |
| Estaban et al. ⁴⁰ 2004 | RCT: passed SBT and within 48 h developed ARF, 21 centers worldwide NIV vs O ₂ therapy | O ₂ therapy | 110 NIV, 111 O ₂ | No difference in re-intubation, mortality greater NIV; much longer time from development of ARF to intubation with NIV |

NIV = noninvasive ventilation
 RCT = randomized controlled trial
 SBT = spontaneous breathing trial
 PSV = pressure support ventilation
 LOS = length of stay
 CHF = congestive heart failure
 APACHE = Acute Physiology and Chronic Health Evaluation
 ARF = acute respiratory failure

18%), ICU LOS (mean \pm SD, 8.9 ± 5.7 d versus 11.6 ± 14.9 d), and hospital LOS (mean \pm SD, 23.3 ± 16.4 d versus 25.5 ± 21.4 d) were not significantly different between the NIV and oxygen therapy groups, respectively.

Similar data were obtained by Ferrer et al.³³ The investigators randomized 162 subjects at high risk to NIV or standard oxygen therapy. ARF developed in 13 of 79 subjects in the NIV group and in 27 of 83 subjects in the oxygen therapy group, $P = .03$.³³ NIV was used as rescue in 19 control subjects, 9 of whom avoided intubation, and in 4 subjects on NIV, all avoided intubation.³³ ICU mortality in the subjects with hypoxemic respiratory failure was lower in the NIV group ($P = .035$); however, hospital mortality was unchanged.³³

Ferrer et al.³⁴ performed a second RCT in this area. They randomized 106 subjects with chronic respiratory failure who passed an SBT and had one of the risk factors outlined above. Again, the development of ARF was the study end point. In the NIV group, 8 of 54 subjects developed ARF, and 25 of 52 subjects in the oxygen therapy group developed ARF ($P < .001$).³⁴ The 90-d mortality was lower in the NIV group than in the oxygen therapy group, $P < .01$.³⁴ Finally, Khilnani et al.³⁵ randomized a group of 40 subjects with severe COPD who were extubated after meeting weaning and extubation criteria to standard oxygen therapy or NIV (20 each group). They observed no differences in the re-intubation rate (NIV group, 15%; oxygen therapy group, 25%), ICU LOS after extubation (NIV group, 2.05 ± 2.15 d; oxygen therapy group, 1.55 ± 0.82 d) or hospital LOS (NIV group, 16.10 ± 6.29 d; oxygen therapy group, 18.25 ± 7.91 d).³⁵

Although the results are mixed, these studies establish the need to use NIV on patients at risk who were extubated after successful completion of an SBT. This should be the standard of care in our ICUs. The use of NIV postextubation in patients at high risk is recommended in the recent guidelines on liberation from mechanical ventilation from the American Thoracic Society and the American College of Chest Physicians.³⁶ Patients at risk clearly have a greater probability of re-intubation than those not presenting with these risk factors, and it has been clearly established that patients who are re-intubated have a higher mortality.^{37,38}

NIV for Extubation Failure, Developing ARF

This group of studies addressed a mixed group of subjects at high and low risk who passed an SBT but within 48 hours developed ARF postextubation. Keenan et al.³⁹ randomized 81 subjects who developed ARF (defined as a breathing frequency of > 30 breaths/min, as an increase in breathing frequency of $> 50\%$, or as use of accessory muscles of respiration or abdominal paradox) to NIV or to standard oxygen therapy. The subjects eventually developed hypercarbic or hypoxemic ARF. The rate of re-intu-

bation was the same between the groups (72% versus 69%), as was the hospital mortality (31% for both groups). In addition, no differences were found in the duration of mechanical ventilation or ICU or hospital LOS.³⁹

Esteban et al.⁴⁰ performed a multi center (21 centers) worldwide study of 221 subjects who were randomized within 48 h after extubation if they met the following criteria: respiratory acidosis ($\text{pH} < 7.35$ and $\text{Pa}_{\text{CO}_2} > 45$ mm Hg), clinical signs suggestive of respiratory muscle fatigue or increased respiratory effort, a breathing frequency > 25 breaths/min for 2 consecutive hours, and hypoxemia ($\text{S}_{\text{pO}_2} < 90\%$ or $\text{Pa}_{\text{O}_2} < 80$ mm Hg, with an $\text{F}_{\text{IO}_2} > 0.50$). The re-intubation rate was the same in each group, 48%; however, the ICU mortality was higher in the NIV group (25%) than in the standard of care group (14%) ($P = .048$).⁴⁰ An explanation for this higher mortality in the NIV group may be because the time from development of respiratory failure to intubation was longer in the NIV group (12 h) compared with the standard of care group (2.5 h) ($P = .02$). It was assumed that subjects on NIV, although gas exchange was good, were working excessively to breathe during the 12-h period.⁴⁰ Thus, potentially developing subject-induced lung injury by the excessive transpulmonary pressure that developed.^{41,42}

Recent data from Yoshida et al.^{43,44} clearly indicate that excessive effort and work of breathing during ventilatory support can induce localized overdistention and lung injury. It is for this reason that it has been highly recommended that, when NIV is applied for hypoxemic ARF, the assessment of the patient's response should occur frequently, and if the patient's clinical status does not improve within the first 1–2 h, he or she should be intubated.⁴⁵ That is, even if gas exchange is normalized but the patient's clinical presentation still indicates severe respiratory distress (rapid breathing frequency, small tidal volume, use of accessory muscles of ventilation, tachycardia, and hypertension), the patient should be intubated.⁴⁵ Thus, the use of therapeutic NIV in postextubation respiratory failure must be questioned. It may be most beneficial for patients to be re-intubated if they develop respiratory failure. If NIV is attempted, then a very low threshold for failure should be established and intubation should not be delayed.

Postoperative Use of NIV

A number of RCTs address the use of NIV postextubation after surgical procedures (Table 3).^{46–54} NIV use after lung resection was studied by 3 groups.^{46,49,52} Aguiló et al.⁴⁶ randomized subjects to receive NIV ($n = 10$) versus oxygen therapy ($n = 9$) after surgery for 1 h. The NIV group demonstrated an increase in Pa_{O_2} , from 68.0 ± 2.7 mm Hg to 76.7 ± 3.0 mm Hg, $P < .05$; the control group showed no change in Pa_{O_2} .⁴⁶ No other differences were noted.

Table 3. Postextubation to NIV: Surgical Subjects

| Study, y | Study Design | Control | Subjects, n | Outcome |
|---|--|------------------------|--|---|
| Lung Resection | | | | |
| Aguiló et al, ⁴⁶ 1997 | RCT: immediately after extubation, subjects were randomized to 1 h of NIV or O ₂ therapy | O ₂ therapy | 10 NIV, 9 O ₂ | NIV group, increase in P _{O₂} after 1 h; standard of care, no change in P _{O₂} |
| Auriant et al, ⁴⁹ 2001 | RCT: postoperative development of hypoxemic ARF; NIV vs O ₂ therapy | O ₂ therapy | 24 NIV 24 O ₂ | Lower re-intubation NIV 90 d lower mortality NIV |
| Perrin et al, ⁵² 2007 | RCT: perioperative randomization to NIV or O ₂ therapy NIV 7 d before surgery and 3 d after surgery | O ₂ therapy | 14 NIV 18 O ₂ | P _{O₂} , FVC, FEV ₁ better with NIV, hospital LOS longer with O ₂ therapy; no difference in postoperative atelectasis |
| Abdominal or thoraco-abdominal surgery | | | | |
| Joris et al, ⁴⁷ 1997 | RCT: after surgery, subjects were randomized to NIV 8 cm H ₂ O pressure support/cm H ₂ O PEEP, NIV 12 cm H ₂ O pressure support/4 cm H ₂ O PEEP and O ₂ therapy for 1 d | O ₂ therapy | 10 NIV 12/4 10 NIV 8/4 10 O ₂ | NIV 12/4 improved FVC, FEV, and S _{pO₂} compared with O ₂ , NIV 8/4 no difference from O ₂ therapy |
| Ebeo et al, ⁵¹ 2002 | RCT: after surgery, subjects were randomized to NIV vs O ₂ therapy; all subjects had BMI > 40 kg/m ² | O ₂ therapy | 9 NIV, 12 O ₂ | FVC, FEV, and S _{pO₂} higher on postoperative days 1 to 3; however, hospital LOS and pulmonary complications had no differences |
| Michelet et al, ⁵³ 2009 | RCT: randomized subjects who developed ARF postextubation NIV vs O ₂ therapy | O ₂ therapy | 36 NIV, 36 O ₂ | NIV fewer re-intubations, lower ARDS rate, ICU LOS, and less anastomotic leakage |
| Jaber et al, ⁵⁴ 2016 | RCT: randomized subjects with hypoxemic ARF within 7 d of surgery to NIV or O ₂ therapy; multi center (20) study | O ₂ therapy | 148 NIV, 145 O ₂ | Fewer re-intubations, less VFD, fewer infections with NIV, no difference in mortality |
| Patients With Transplantation | | | | |
| Antonelli et al, ⁴⁸ 2000 | RCT: randomized subjects developed hypoxemic respiratory failure after surgery to NIV vs O ₂ therapy | O ₂ therapy | 20 NIV, 20 O ₂ | Re-intubation lower NIV ICU LOS lower NIV, ICU mortality lower NIV, hospital mortality no difference |
| Rocco et al, ⁵⁰ 2001 | Case series: subjects who developed ARF postextubation after lung transplantation, received NIV | ND | 21 | 86% of patients avoided re-intubation; 19 of 21 survived the ICU |

NIV = noninvasive ventilation
 RCT = randomized controlled trial
 ARF = acute respiratory failure
 LOS = length of stay
 BMI = body mass index
 VFD = ventilator free days
 ND = no data

Auriant et al⁴⁹ performed an RCT of subjects with postoperative lung resection who developed acute hypoxemic respiratory failure. The subjects were randomized to NIV or oxygen therapy. In the NIV group, 5 of 24 subjects required intubation versus 12 of 24 in the standard of care group, $P = .035$.⁴⁹ Mortality at 120 d was 9 subjects in the standard care group versus 3 in the NIV group $P = .045$.⁴⁹ All other outcomes were similar between the groups. Perrin et al⁵² compared NIV ($n = 14$) with standard of care ($n = 18$) before and after surgery in subjects who received elective lobectomy for lung cancer. The subjects were enrolled if their FEV₁ was <70% before surgery.⁵² The subjects in the NIV group received NIV 7 d before surgery at home and 3 d after surgery; the control group received no preoperative therapy, only postextubation oxygen therapy.⁵² Two hours after surgery and up until the third day postoperative P_{aO₂}, FVC, and FEV₁ were significantly better in the NIV group; hospital LOS was longer in the control group, $P = .04$, and the incidence of postoperative atelectasis was 14.2% in the NIV group versus 38.9% in the control group, $P = .15$.⁵²

The largest group of subjects studied were those who required abdominal or thoraco-abdominal surgery.^{47,51,53,54} Joris et al⁴⁷ compared the use of NIV at 8 cm H₂O of pressure support over 4 cm H₂O of PEEP ($n = 10$) and 4 cm H₂O of pressure support over 4 cm H₂O of PEEP ($n = 10$) to oxygen therapy ($n = 10$) in subjects after gastropasty. The bi-level positive airway pressure at 12 cm H₂O Pressure support 4 cm H₂O PEEP significantly improved FVC, FEV₁, and S_{pO₂} on postoperative day 1 compared with oxygen therapy; bi-level positive airway pressure at 8 cm H₂O pressure support 4 cm H₂O PEEP had no significant effect on any measured variable.⁴⁷ No outcome data were presented. After gastric surgery for subjects with obesity (body mass index > 40 kg/m²), Ebeo et al⁵¹ randomized subjects to bi-level positive airway pressure ($n = 9$) for the first 24 h or to oxygen therapy ($n = 12$). FVC, FEV₁, and S_{pO₂} were significantly higher in the bi-level positive airway pressure group over postoperative days 1 to 3; however, hospital days and postoperative pulmonary complication were similar between the groups.⁵¹

Michelet et al⁵³ performed a matched case-control study of subjects after esophagectomy who developed ARF. NIV was applied to 36 subjects, and oxygen therapy was used in 36 subjects. The NIV group had fewer re-intubations (9 versus 23, $P = .008$), a lower frequency of ARDS (8 versus 19, $P = .02$), ICU LOS (14[13] d versus 22[18] d, $P = .01$), and anastomotic leakage was less in the subjects who received NIV (2 versus 10, $P = .03$).⁵³ Most recently, Jaber et al,⁵⁴ in a multi-center RCT (20 centers), randomized subjects with acute hypoxemic respiratory failure after abdominal surgery to NIV ($n = 148$) or standard oxygen therapy ($n = 145$). Hypoxemic ARF was defined as

P_{aO₂} < 60 mm Hg or S_{pO₂} < 90% when breathing room air or P_{aO₂} < 80 mm Hg when breathing 15 L/min of oxygen plus either a frequency of >30 breaths/min or clinical signs of “intense” respiratory muscle work and/or increased work of breathing within 7 d of the surgical procedure.⁵⁴ Re-intubation occurred in 33.1% of the NIV group versus 45.5% of the subjects in the O₂ therapy group, $P = .03$.⁵⁴ NIV resulted in more intensive ventilator-free days (23.2 versus 25.4 d, $P = .04$). Also, fewer subjects in the NIV group developed health-care-related infections (31.4% versus 49.2%, $P = .003$); however, there were no significant differences in 90-d mortality (14.9% in the NIV group versus 21.5% in the O₂ group, $P = .15$) and gas exchange.⁵⁴

There are 2 trials that focused on subjects with transplantations.^{48,50} Antonelli et al,⁴⁸ randomized subjects who developed acute hypoxemic respiratory failure after solid-organ transplantation to NIV ($n = 20$) or oxygen therapy ($n = 20$). A sustained improvement in P_{aO₂}/F_{IO₂} was observed in 12 subjects in the NIV group versus 5 in the standard of care group, $P = .03$.⁴⁸ The re-intubation rate was lower in the NIV group (20%) versus the standard of care group (70%), $P = .002$; ICU LOS was greater in the standard of care group versus the NIV group (9[4] d, versus 5.5[3] d, $P = .03$) and ICU mortality was lower in the NIV group (20% versus 50%, $P = .05$); however, hospital mortality did not differ.⁴⁸ Rocco et al⁵⁰ reported a similar result in subjects after lung transplantation. In a case series in which 21 subjects who developed ARF were managed with NIV, 86% of the subjects avoided re-intubation, and a total of 19 of 21 subjects survived the ICU.⁵⁰

Summary of Postoperative Use of NIV

Although the data on the use of NIV in the postoperative setting are mixed, the majority of the studies demonstrate a positive impact of NIV on postoperative complication, the re-intubation rate, and ICU LOS. As a result, NIV is indicated for the management of the postoperative patient. This is especially true in patients after abdominal procedures in which the impact on respiratory function after surgery is greatest. The use of NIV in these settings is supported by recent systematic reviews^{15,55} and by the recent guidelines of the European Respiratory Society/American Thoracic Society.⁵⁶ Although these guidelines specifically recommend use of NIV in the setting of ARF after intubation; prophylactic use after extubation is not mentioned.

CPAP Postextubation After Surgery

The vast majority of the data on the use of CPAP postextubation is after surgery (Tables 4 and 5). There have been a number of RCTs that addressed the use of CPAP

Table 4. Postextubation CPAP: Cardiac, Vascular, and Bariatric Surgical Subjects

| Study, y | Study Design | Control | Subjects, n | Outcome |
|--|---|---------------------------------------|---|--|
| Failed Spontaneous Breath Trial | | | | |
| Pinilla et al, ⁵⁷ 1990 | RCT: randomized postoperative subjects to CPAP vs O ₂ therapy for 12 h | O ₂ therapy | 32 CPAP, 26 O ₂ | Initially, P _{O₂} increased with CPAP but, by 24 h, there was no difference; atelectasis, no difference |
| Thomas et al, ⁵⁸ 1992 | RCT: randomized postoperative subjects to 1 h CPAP at 5 cm H ₂ O postextubation vs O ₂ therapy | O ₂ therapy | 14 CPAP, 14 standard of care | Initially, oxygenation improved with CPAP but no difference in any outcome variable |
| Jousela et al, ⁵⁹ 1994 | RCT: randomized subjects to 1 h CPAP 10 cm H ₂ O postextubation vs O ₂ therapy | O ₂ therapy | 15 CPAP, 15 O ₂ | Oxygenation initially improved with CPAP but, by day 2, no difference; no difference in atelectasis |
| Pasquina et al, ⁶⁰ 2004 | RCT: randomized subjects to NIV vs CPAP after surgery; both therapies were applied for 30 min, 4 times/d; PEEP for both groups at 5 cm H ₂ O | NIV | 75 CPAP, 75 NIV | At ICU discharge, no difference in oxygenation, PFTs, ICU LOS; atelectasis score improved more in patients on NIV |
| Zarbock et al, ⁶¹ 2009 | RCT: randomized subjects after surgery to continuous CPAP 10 cm H ₂ O vs CPAP 10 cm H ₂ O 10 min every 4 h, both for 6 h | CPAP 10 cm H ₂ O every 4 h | 236 CPAP every 4 hours vs 232 CPAP continuously | Continuous CPAP decreased pulmonary complications and ICU readmission and improved oxygenation |
| Vascular surgery | | | | |
| Böhner et al, ⁷⁰ 2002 | RCT: randomized subjects after surgery to CPAP 10 cm H ₂ O vs O ₂ therapy | O ₂ therapy | 99 standard of care, 105 CPAP | Severe oxygenation problems reduced with CPAP but no difference in pulmonary complications, ICU or hospital LOS, and mortality |
| Bariatric surgery | | | | |
| Neligan et al, ⁷¹ 2009 | RCT: randomized subjects after surgery to CPAP 10 cm H ₂ O vs O ₂ therapy, all morbidly obese | O ₂ therapy | 20 CPAP, 20 O ₂ | PFTs improved faster with CPAP; pulmonary complications not followed up |
| Gaszynski et al, ⁷² 2007 | RCT: randomized subjects after surgery to CPAP 10 cm H ₂ O vs O ₂ therapy | O ₂ therapy | 10 CPAP, 9 O ₂ | Oxygenation improved with CPAP but no other outcome was provided |

RCT = randomized controlled trial
NIV = noninvasive ventilation
PFT = pulmonary function test
LOS = length of stay

Table 5. Postextubation CPAP: Abdominal and/or Thoracic Abdominal Surgical Subjects

| Study, <i>y</i> | Study Design | Control | Subjects, <i>n</i> | Outcome |
|--|---|--|---|---|
| Failed Spontaneous Breath Trial | | | | |
| Carlsson et al, ⁶² 1981 | Randomized postoperative subjects to every 4 h of CPAP vs every 4 h face mask O ₂ therapy; the first 5 subjects had CPAP 5 cm H ₂ O, the rest had 10 cm H ₂ O | O ₂ therapy | 13 CPAP, 11 O ₂ | No difference on any physiologic variable |
| Ricksten et al, ⁶³ 1986 | Randomized postoperative subjects to CPAP, PEP, or incentive spirometry for 30 breaths every 4 h while awake for 3 d | Incentive spirometry | 13 CPAP, 15 PEP, 15 incentive spirometry | Oxygenation improved with CPAP and PEP; FVC higher CPAP and PEP; atelectasis less CPAP and PEP |
| Lindner et al, ⁶⁴ 1987 | Randomized postoperative subjects to CPAP 12 cm H ₂ O for 1 h after extubation, then 3 h per day for the first 5 postoperative days vs O ₂ therapy | O ₂ therapy | 17 CPAP, 17 O ₂ | VC, IRV, ERV, and FRC increased with CPAP; no outcomes provided |
| Denehy and Carroll ⁶⁵ 2001 | Randomized postoperative subjects to CPAP 10 cm H ₂ O for 15 min 4 times per day, CPAP 10 cm H ₂ O for 30 min 4 times per day, and physiotherapy 4 times per day; all groups received physiotherapy 4 times per day | Physiotherapy | 15 CPAP 15 min, 15 CPAP 30 min, 18 physiotherapy | No difference in any of the PFT results or oxygenation among the groups |
| Olsen et al, ⁶⁶ 2002 | Randomized postoperative subjects to CPAP vs breathing exercises | Breathing exercises | 34 CPAP, 36 breathing exercises | Re-intubation and prolonged mechanical ventilation were fewer and shorter in the CPAP group; no other differences were observed |
| Squadrone et al, ⁶⁷ 2005 | Randomized postoperative subjects to CPAP vs O ₂ therapy, CPAP 7.5 cm H ₂ O, F _{IO₂} 0.50; air-entrainment mask F _{IO₂} 0.50 both for 6 h | O ₂ therapy | 104 O ₂ , 105 CPAP | CPAP group, lower re-intubation, pneumonia infection, and sepsis |
| Kindgen-Milles et al, ⁶⁸ 2005 | Randomized postoperative subjects to 10 cm H ₂ O CPAP continuously vs standard of care plus CPAP 10 cm H ₂ O, 10 min every 4 h | Standard of care plus 10 cm H ₂ O CPAP 10 min every 4 h | 25 continuous CPAP, 25 standard of care plus CPAP every 4 h | Continuous CPAP had fewer pulmonary complications; hospital LOS was shorter with continuous CPAP |
| Stock et al, ⁶⁹ 1985 | Randomized postoperative subjects to 10 cm H ₂ O CPAP vs incentive spirometry vs cough and deep breath | Cough and deep breath | 23 CPAP, 22 incentive spirometry, 20 cough and deep breath | No differences in any outcome |

PEP = peak expiratory pressure

VC = vital capacity

IRV = inspiratory reserve volume

ERV = expiratory reserve volume

FRC = functional residual volume

PFT = pulmonary function testing

LOS = length of stay

after cardiac surgery,⁵⁷⁻⁶¹ abdominal and/or thoracic surgery,⁶²⁻⁶⁹ vascular surgery,⁷⁰ and bariatric surgery.^{71,72}

CPAP Postextubation in Subjects After Cardiac Surgery

Pinilla et al⁵⁷ randomized subjects who had postoperative coronary artery bypass to receive CPAP ($n = 32$) versus standard of care ($n = 26$). All the subjects were ventilated with 5 cm H₂O PEEP for ~18 h, then 5 cm H₂O face mask CPAP or oxygen therapy for 12 h after extubation.⁵⁷ Initially P_{aO_2} was significantly increased in the CPAP group, but, by 24 h postextubation, there was no difference in P_{aO_2} ; there also was no difference in the development of atelectasis.⁵⁷ Thomas et al⁵⁸ and Jousela et al⁵⁹ performed similar studies in subjects who were postoperative coronary artery bypass. Subjects in the study by Thomas et al⁵⁸ were randomized to 1 h of 5 cm H₂O CPAP postextubation ($n = 14$) or to oxygen therapy ($n = 14$). Initially, the oxygenation status was better in the CPAP group, but there were no differences on any outcome variable.⁵⁸

In the study by Jousela et al,⁵⁹ the subjects were also randomized to CPAP ($n = 15$) or oxygen therapy ($n = 15$) after extubation, but CPAP was applied at 10 cm H₂O. As with the studies by Pinilla et al⁵⁷ and Thomas et al,⁵⁸ in the study by Jousela et al,⁵⁹ the CPAP group responded with improved oxygenation, but, by day 2, this improvement was lost and there again was no difference in the development of atelectasis. Pasquina et al⁶⁰ compared the benefit of NIV ($n = 75$) with CPAP ($n = 75$) in subjects who were postoperative coronary artery bypass. Both techniques were applied for 30 min, 4 times per day. PEEP in both groups was 5 cm H₂O, and NIV was adjusted to provide a tidal volume of 8–10 mL/kg. At ICU discharge, there were no differences in oxygenation, pulmonary function tests, or LOS; however, the atelectasis score improved in 60% of subjects in the NIV group versus 40% in the CPAP group ($P = .02$).⁶⁰

The most convincing study regarding the use of CPAP after coronary artery bypass was by Zarbock et al.⁶¹ They compared 10 cm H₂O CPAP given for 10 min every 4 h ($n = 236$) with continuous CPAP at 10 cm H₂O for 6 h ($n = 232$).⁶¹ The continuous CPAP group had improved oxygenation and fewer pulmonary complications (12/232 versus 25/236, $P = .03$). The ICU readmission rate was also lower in the continuous CPAP group (7/232 versus 14/236 subjects, $P = .03$).⁶¹

The analyses of these data have not had a widespread affect on the postoperative management of the patient with a coronary artery bypass. It is infrequent that these patients will receive prophylactic continuous CPAP. The application of CPAP is more likely in select postoperative patients who present with significant comorbidities or gas

exchange problems than the widespread prophylactic application to all patients.

CPAP Postextubation in Abdominal and/or Thoracic Surgical Subjects

The data on the use of CPAP in subjects with postoperative abdominal and/or thoracic surgery is split (Table 5). Earlier studies showed negative results^{62,65,69} but more-recent studies demonstrate the beneficial effects of CPAP.^{63,64,66-68} Carlsson et al⁶² randomized subjects to CPAP (5 or 10 cm H₂O) for 4 h ($n = 13$) versus oxygen therapy ($n = 11$). No differences of any type were observed between the two groups. Similar data were observed by Denehy and Carroll⁶⁵ and Stock et al⁶⁹. Denehy and Carroll⁶⁵ compared the effect of CPAP 10 cm H₂O given for 15 min ($n = 17$) or 30 min ($n = 15$) 4 times per day for the first 3 postoperative days to physiotherapy twice daily ($n = 18$). All 3 groups received physiotherapy daily. The use of CPAP did not affect any clinical or physiologic variable. Stock et al⁶⁹ compared CPAP with incentive spirometry and with cough and deep breathing but observed no differences among the 3 groups.

The first study to our knowledge to find benefit of CPAP in subjects with postoperative abdominal surgery was the study by Ricksten et al.⁶³ They compared the effects of 10-15 cm H₂O CPAP ($n = 12$) with that of positive expiratory pressure therapy ($n = 15$) and incentive spirometry ($n = 15$). CPAP, positive expiratory pressure therapy, and incentive spirometry were administered for 30 breaths every hour while awake for 3 d. CPAP and positive expiratory pressure therapy resulted in better oxygenation and a lower incidence of atelectasis than with the incentive spirometry group. Lindner et al⁶⁴ also found CPAP ($n = 17$) superior to the standard of care ($n = 17$). They randomized subjects to 12 cm H₂O CPAP for 1 h after extubation and then 3 h a day for the first 5 postoperative days. Vital capacity, inspiratory reserve volume, expiratory reserve volume, and functional residual capacity were all significantly increased in the CPAP group. However, there were no differences in postoperative pulmonary complications.

Olsen et al⁶⁶ randomized subjects to 5-10 cm H₂O CPAP ($n = 34$) versus breathing exercises by inspiratory resistance positive expiratory pressure therapy ($n = 36$). Reintubation and prolonged mechanical ventilation were higher in the inspiratory resistance positive expiratory pressure therapy group (7 of 36) versus CPAP (1 of 34), $P < .05$.⁶⁶ All other comparisons were not significantly different. The largest and most definitive trial was that performed by Squadrone et al.⁶⁷ They randomized subjects to receive oxygen therapy ($n = 104$) versus CPAP ($n = 105$). Oxygen therapy was administered via 50% air-entrainment mask for 6 h and CPAP at 7.5 cm H₂O and 50% oxygen for 6 h.⁶⁷ After 6 h, both groups were transitioned

to a 30% air-entrainment mask for 1 h and their P_{aO_2}/F_{IO_2} was evaluated.⁶⁷ If the ratio was <300 mm Hg, then the subjects were placed back on the study settings, but if the ratio was >300 mm Hg, then treatment was stopped.⁶⁷ If the subjects did not tolerate either arm of the study, then they were given a nasal cannula at 8–10 L/min. The CPAP group had a lower re-intubation rate (1% versus 10%, $P = .005$), and a lower rate of pneumonia (2% versus 10%, $P = .02$), infection (3% versus 10%, $P = .03$), and sepsis (2% versus 9%, $P = .03$).⁶⁷

Kindgen-Milles et al⁶⁸ randomized subjects to 10 cm H₂O continuous CPAP ($n = 25$) versus standard of care plus 10 cm H₂O CPAP for 10 min every 4 h ($n = 25$). The use of continuous CPAP resulted in fewer pulmonary complications (7 of 25 versus 24 of 25, $P = .019$) and shorter hospital LOS (22 ± 2 d vs 34 ± 5 d, $P = .048$), whereas ICU LOS trended shorter (8 ± 1 d versus 12 ± 2 d) but not significantly.⁶⁸

The studies by Squadrone et al⁶⁷ and Kindgen-Milles et al⁶⁸ provide strong support for the use of CPAP postextubation in patients after abdominal surgery, similar to the beneficial effects of NIV in this population. The use of CPAP in these patients is supported by recent systematic reviews^{15,55} and guidelines.⁵⁶ However, again, widespread prophylactic application of CPAP postextubation in all patients with abdominal surgery is lacking. As with NIV application, CPAP seems to be reserved for patients who present with a high risk for re-intubation and ARF.

CPAP Postextubation, Vascular Surgery

Only one study, by Bohner et al,⁷⁰ was identified. They studied the effects of CPAP 10 cm H₂O ($n = 99$) versus oxygen therapy ($n = 105$) in subjects who required mid-line laparotomy for vascular surgery. Severe oxygenation problems were reduced with CPAP (95 versus 17 subjects, $P = .01$), but there were no differences in pulmonary complications, ICU or hospital LOS, or mortality.

CPAP After Bariatric Surgery

Neligan et al⁷¹ and Gaszynski et al⁷² studied the use of CPAP after bariatric surgery. Neligan et al⁷¹ randomized subjects to CPAP ($n = 20$) provided by the Boussignac valve at 9.4 cm H₂O or to oxygen therapy ($n = 20$). Pulmonary function improved significantly faster in the CPAP group than in the oxygen therapy group. However they did not follow up postoperative pulmonary complications. Gaszynski et al⁷² randomized 19 subjects who were morbidly obese to CPAP ($n = 10$) or to standard of care ($n = 9$), with CPAP again provided by the Boussignac valve at 9.4 cm H₂O. The subjects who received CPAP had a higher P_{aO_2} at 30 min, 4 h, and 8 h postextubation than the standard of care group (mean \pm SD of all time

points 81.0 ± 16.0 mm Hg versus 65 ± 4.9 mm Hg, $P < .05$). No other outcomes were indicated.

These 2 studies were mostly negative because of the level of CPAP applied. Patients who are morbidly obese require a high level of PEEP to stabilize the lung, and the 9.4 cm H₂O CPAP used in these studies was most likely inadequate.^{73,74} Postoperative patients who are morbidly obese are the most in need of noninvasive ventilatory support postextubation. The use of CPAP in the 10–15 cm H₂O range for management of sleep apnea should be applied to all of these patients immediately postextubation and slowly decreased over the next 24–48 h. But again, widespread application of prophylactic CPAP in this group is lacking.

Summary of CPAP Postextubation After Surgery

In 2010, Chiumello et al³ identified 29 clinical trials associated with the use of NIV or CPAP in the surgical postextubation setting. In 15 of 22 prophylactic studies and 4 of 7 therapeutic studies in which noninvasive ventilatory support was provided, gas exchange improved. Re-intubation was reduced in 11 of the total 29 studies, but other outcomes were improved in only 1 study. In spite of this limited benefit, they recommend the use of NIV or CPAP postextubation in surgical patients, with similar recommendations made by Jaber et al⁵⁵ in 2014. Most recently, in 2017, the European Respiratory Society/American Thoracic Society guidelines⁵⁶ recommended the use of NIV or CPAP for postoperative respiratory failure. Clearly, the use of NIV and/or CPAP in postoperative respiratory failure is indicated, but the prophylactic application of NIV and/or CPAP should be considered primarily in patients at high risk of re-intubation. The definition of high risk has varied in the literature, but most clinicians would agree that patients with a history of COPD or congestive heart failure, body mass index > 40 kg/m², age > 65 y, multiple SBT failures, excessive secretions, and upper-airway obstruction meet the definition.^{9,10}

HFNC Postextubation in Surgical Subjects

A number of clinical trials that addressed the use of HFNC postextubation in surgical subjects have been performed (Tables 6 and 7). General surgical populations,^{73,74} renal transplantation recipients,⁷⁵ major abdominal surgery subjects,⁷⁶ and cardiac surgical subjects^{77–79} were studied.

Dhillon et al⁷⁵ retrospectively reviewed surgical cases with ARF postextubation from August 2015 to February 2016. They identified 46 subjects managed with HFNC, and 138 well-matched subjects managed with cool mist nasal cannula. Before extubation, the subjects with HFNC had a longer length of mechanical ventilation (7.1 versus 3.4 mean d, $P < .01$) and ICU stay (7.8 versus 4.1 mean d, $P < .01$).⁷⁵ The raw re-intubation rates were similar between the 2 groups;

Table 6. Postextubation HFNC: General Surgical Subjects

| General Surgical Studies, y | Study Design | Control | Subjects, n | Outcome |
|--------------------------------------|--|-------------------------|---------------------------------------|--|
| Dhillon et al, ⁷⁵ 2017 | Retrospectively reviewed surgical cases (Apr 2015 to Feb 2016); matched subjects with HFNC vs cool mist nasal cannula | Cool mist–nasal cannula | 145 HFNC, 138 cool mist nasal cannula | HFNC group had a longer duration of mechanical ventilation and ICU LOS before extubation; raw data re-intubation no difference, multi-variable analysis showed lower re-intubation with HFNC |
| Tirvoipati et al, ⁷⁶ 2010 | RCT: postextubation randomized stable subjects to HFNC 30 min then HFFM 30 min vs HFFM 30 min then HFNC 30 min | HFFM 30 min | 25 HFNC first, 25 HFFM first | No difference in any clinical variable but greater subject tolerance with HFNC; no outcome data provided |
| Tu et al, ⁷⁷ 2017 | Retrospectively reviewed subjects with renal transplantation (Jul 2011 to Sep 15) who developed postextubation hypoxemic ARF compared matched subjects NIV vs HFNC | NIV | 20 HFNC, 18 NIV | Fewer ventilator-free days with HFNC, pneumothorax and skin breakdown less HFNC, mortality 1 HFNC vs 4 NIV |
| Futier et al, ⁷⁸ 2016 | Randomized subjects after abdominal surgery with moderate-to-high risk of postoperative complications to prophylactic HFNC or O ₂ therapy | O ₂ therapy | 108 HFNC, 112 O ₂ | 1 h postextubation, no difference in oxygenation and no difference in pulmonary complications over 7 d after surgery |

HFNC = high-flow nasal cannula
 RCT = randomized controlled trial
 HFFM = high flow face mask
 ARF = acute respiratory failure
 NIV = noninvasive ventilation

Table 7. Postextubation HFNC: Cardiac Surgical Subjects

| Lung Resection Studies, y | Study Design | Control | Subjects, n | Outcome |
|-----------------------------------|---|-------------------------------|---|--|
| Parke et al, ⁷⁹ 2013 | Randomized postoperative subjects to HFNC vs simple O ₂ therapy for the first 2 d | Simple O ₂ therapy | 169 HFNC, 171 Simple O ₂ therapy | Postoperative Day 3 oxygenation better with HFNC, need to escalate to high level of care less HFNC |
| Stéphan et al, ⁸⁰ 2015 | Randomized subjects who developed ARF after surgery to HFNC vs NIV | NIV | 414 HFNC, 416 NIV | No difference in re-intubation rate, gas exchange, or pulmonary complication |
| Corley et al, ⁸¹ 2015 | Randomized postoperative subjects to HFNC vs simple O ₂ therapy, all subjects had BMI > 30 kg/m ² | Simple O ₂ therapy | 81 HFNC, 74 simple O ₂ therapy | No difference in atelectasis, oxygenation, or breathing frequency |

HFNC = high-flow nasal cannula
 ARF = acute respiratory failure
 NIV = noninvasive ventilation
 BMI = body mass index

however, multivariate analysis indicated a lower intubation rate with HFNC ($P = .02$). Tiruvoipati et al⁷⁶ randomly compared 2 protocols in a general surgical population: high-flow face mask for 30 min, followed by HFNC for 30 min ($n = 25$); and HFNC for 30 min, followed by high-flow face mask for 30 min ($n = 25$), each applied in stable subjects after extubation.⁷⁶ There were no significant differences in gas exchange, respiratory, or cardiovascular variables; however, there was greater subject tolerance with HFNC ($P = .01$) and a trend toward better comfort ($P = .09$), although no outcome variables were evaluated.⁷⁶

Tu et al⁷⁷ retrospectively reviewed data from subjects with renal transplantation from July 2011 to September 2015, who developed acute hypoxemic respiratory failure postextubation. A total of 38 subjects were identified, including 20 who received HFNC and 18 who received NIV. One subject in the HFNC group versus 4 in the NIV group died ($P = .008$). Ventilator-free days at hospital day 28 were 26 ± 3 HFNC group versus 21 ± 3 NIV group ($P < .001$). The incidence of pneumothorax (0% versus 22%, $P = .042$) and skin breakdown (0% versus 22.2%, $P = .042$) were lower in the HFNC group. Futier et al⁷⁸ randomized subjects with major abdominal surgery and with a moderate-to-high risk of postoperative pulmonary complications to prophylactic application of HFNC ($n = 108$) versus oxygen therapy ($n = 112$). The primary outcome was hypoxemia at 1 postextubation and after treatment discontinuation. At 1 h postextubation, 23 subjects with HFNC versus 27 subjects with oxygen therapy developed hypoxemia, and 29 subjects with HFNC versus 34 subjects with oxygen therapy developed hypoxemia after discontinuation of therapy ($P = .58$). Pulmonary complications over the 7 d postextubation did not differ between the groups nor did any other secondary outcomes.

HFNC in Postextubation Cardiac Surgical Subjects

The first RCT that evaluated the use of HFNC in subjects with cardiac surgery was performed by Parke et al.⁷⁹ They randomized subjects to HFNC ($n = 169$) versus oxygen therapy ($n = 171$) for the first 2 d postextubation. The primary outcome was the number of subjects with a $S_{pO_2}/F_{IO_2} > 445$ after day 2.⁷⁹ On day 3, the S_{pO_2}/F_{IO_2} was > 445 in 46.4% of the subjects on HFNC versus 42.4% of the subjects on oxygen therapy, $P = .45$.⁷⁹ Escalation of respiratory support (use of NIV, CPAP, high-flow face mask, or oxygen therapy after trial discontinuation) occurred in 27.8% of subjects on HFNC versus 45% of subjects on oxygen therapy ($P = .001$), but no long-term outcomes differed.⁷⁹

Stephan et al⁸⁰ compared the use of HFNC ($n = 414$) versus NIV ($n = 416$) in subjects after cardiac surgery who developed ARF in a noninferiority study conducted in 6 French ICUs. HFNC was not inferior to NIV. Treatment failed in 91 of 416 in the NIV group versus 87 of 414 subjects in the HFNC group. Re-intubation was required in

57 subjects on NIV versus 58 subjects on HFNC.⁸⁰ Gas exchange and postoperative pulmonary complications were similar in the 2 groups, and no difference in ICU mortality was noted (23 in the NIV group versus 28 in the HFNC group).⁸⁰ Corley et al⁸¹ evaluated the use of HFNC ($n = 81$) versus oxygen therapy ($n = 74$) immediately after extubation in subjects who had cardiac surgery and with a body mass index $> 30 \text{ kg/m}^2$. No differences in the primary outcome of atelectasis were noted on day 1 or day 5. There also were no differences in oxygenation or breathing frequency between the groups.⁸¹

Summary of HFNC in Surgical Subjects

Analysis of the current data available does not indicate that HFNC is superior to any other postextubation ventilatory support in surgical subjects. However, HFNC is not inferior to any of these techniques. Subject tolerance and comfort is clearly better with HFNC. The HFNC is more comfortable than a tight fitting mask and, as a result, may be a better choice than other approaches. A special comment regarding patients who are obese is indicated; I would not expect an HFNC to have any marked effect on atelectasis in this population because of the low level of PEEP established with an HFNC.²⁵⁻²⁸ When considering the level of PEEP needed in these patients during mechanical ventilation^{73,74} and the fact that many have sleep apnea that requires nocturnal CPAP well over 10 cm H₂O, therapy that provides a consistent and high CPAP level is indicated, not HFNC.^{82,83}

HFNC Postextubation in General ICU Populations

Rittayamai et al⁸⁴ randomized subjects after extubation from a general ICU population to 2 protocols: HFNC for 30 min followed by a non-rebreathing mask for 30 min ($n = 9$), and a non-rebreathing mask for 30 min followed by HFNC for 30 min ($n = 8$). HFNC resulted in less dyspnea ($P = .04$) and a lower breathing frequency ($P = .009$) and heart rate ($P = .006$); however, no outcome variables were evaluated.⁸⁴ A higher percent of subjects preferred the HFNC to the high-flow face mask (88% to 12%).⁸⁴ Maggiore et al⁸⁵ randomized subjects to HFNC ($n = 53$) versus an air-entrainment mask ($n = 52$) immediately after extubation. After 24 h, the estimated P_{aO_2}/F_{IO_2} values were higher with HFNC ($287 \pm 74 \text{ mm Hg}$ versus $247 \pm 81 \text{ mm Hg}$, $P = .03$).⁸⁵ Interface displacement (32% versus 56%, $P = .001$), oxygen desaturations (40% versus 70%, $P < .001$), and reintubations (4% versus 21%, $P = .01$) as well as any form of additional ventilatory support (7% versus 35%, $P < .001$) were all less frequent with HFNC.⁸⁵ Discomfort was greater in the air-entrainment mask group.⁸⁵ Brotfain et al⁸⁶ retrospectively reviewed 67 subjects after extubation in a 1-y period. The subjects were grouped into those who received HFNC

($n = 34$) versus a non-rebreathing mask ($n = 33$).⁸⁶ The use of HFNC resulted in improved P_{aO_2}/F_{IO_2} after extubation, $P < .05$, and there were more ventilator-free days in the HFNC group (mean \pm SD, $4.14 \pm 2.2 \text{ d}$ versus $3.0 \pm 2.0 \text{ d}$, $P = .03$), and fewer subjects who required intubation (1 versus 6, $P = .04$); here were no differences in ICU LOS or mortality.⁸⁶ Table 8.

Hernandez et al^{87,88} evaluated the impact of HFNC immediately after extubation in 2 separate groups of subjects, those at high risk for re-intubation⁸⁷ and those at low risk of re-intubation.⁸⁸ The variables used to separate the subjects into low versus high risk are outlined in Table 9. Essentially, all the subjects extubated in the 3 participating ICUs were allocated into 1 of the 2 groups. In the high-risk group, the subjects were randomly allocated to receive HFNC ($n = 290$) versus NIV ($n = 314$) for 24 h immediately after extubation.⁸⁷ Re-intubation was not required in 66 subjects in the HFNC group and 60 subjects in the NIV group, with no significant difference.⁸⁷ Postextubation respiratory failure was experienced in 76 subjects in the HFNC group and 125 subjects in the NIV group (95% CI [Confidence interval] 12.9, 6.6 to ∞).⁸⁷ Postextubation LOS was less in the HFNC group (3 [interquartile range, 1-7] d versus 4 [interquartile range, 2-9] d, $P = .048$).⁸⁷ Other outcomes were similar, including mortality. Adverse events that required withdrawal of therapy were noted in 42.9% of the subjects in the NIV group and 0% of the subjects in the HFNC group, $P = .001$.⁸⁷ In the second study by Hernández et al,⁸⁸ subjects at low risk of re-intubation were randomized to HFNC ($n = 264$) versus standard oxygen therapy ($n = 263$). Re-intubation within 72 h was more common in the standard oxygen therapy group (12.2% versus 4.9%, $P = .004$), as was postextubation respiratory failure (14.4% versus 8.3%, $P = .03$).⁸⁸ ICU and hospital LOS, mortality, and adverse events were similar between the 2 groups.

The final RCT in this category was by Fernandez et al.⁸⁹ The investigators randomized subjects immediately after extubation who were at high risk for re-intubation to either HFNC or to standard oxygen therapy. The study was stopped early because of low recruitment, with 78 subjects randomized to HFNC and 77 to standard oxygen therapy. Postextubation respiratory failure developed in 20% of subjects who received HFNC versus 27% who received standard oxygen therapy, $P = .2$.⁸⁹ Re-intubation occurred in 9 subjects in the HFNC group versus 12 subjects in the standard oxygen therapy group, $P = .5$; no differences were found in ICU or hospital LOS or in mortality.⁸⁹

Summary of HFNC in Postextubation Subjects in General ICU

There is no question that the use of HFNC immediately after extubation in patients at high risk of re-intubation is

Table 8. Postextubation HFNC: Subjects in General ICU

| Study, y | Study Design | Control | Subjects, n | Outcome |
|--------------------------------------|---|----------------------|---|---|
| Rittayamai et al, ⁸⁴ 2014 | RCT: randomized subjects postextubation to HFNC for 30 min then to non-rebreathing mask for 30 min vs non-rebreathing mask for 30 min then to HFNC for 30 min | HFNC | 9 HFNC first 8 non-rebreathing mask first | HFNC less dyspnea, lower frequency and HR; no outcome variables evaluated |
| Maggiore et al, ⁸⁵ 2014 | RCT: randomized postoperative subjects to HFNC vs air-entrainment mask | Air-entrainment mask | 53 HFNC, 52 air-entrainment mask | Interface displacement, re-intubation, less need for additional respiratory support all less with HFNC |
| Brofain et al, ⁸⁶ 2014 | Retrospectively reviewed subjects postextubation for 1 y, received HFNC vs non-rebreathing mask | Non-rebreathing mask | 34 HFNC, 33 non-rebreathing mask | HFNC improved oxygenation, more ventilator-free days, fewer re-intubations; no difference in ICU LOS or mortality |
| Hernández et al, ⁸⁷ 2016 | RCT: randomized postoperative subjects to HFNC vs NIV; all the subjects were at high risk for re-intubation | NIV | 290 HFNC, 314 NIV | No difference in the re-intubation rate or mortality; post-randomization ICU LOS less HFNC, HFNC withdrawal of Rx none vs 42.9% NIV group |
| Hernández et al, ⁸⁸ 2016 | RCT: randomized postoperative subjects to HFNC vs simple nasal cannula; all the subjects were low risk for re-intubation | Simple nasal cannula | 264 HFNC, 263 simple nasal cannula | Re-intubation at 72 h after extubation, less HFNC 4.9% vs 12.2% O ₂ ; postextubation respiratory failure less HFNC |
| Fernandez et al, ⁸⁹ 2017 | RCT: randomized subjects at high risk for re-intubation who were not hypercapnic to HFNC cannula vs simple nasal cannula | Simple nasal cannula | 78 HFNC, 77 simple nasal cannula | No difference in any outcome variable evaluated |

HFNC = high-flow nasal cannula
 RCT = randomized controlled trial
 HFNC = high flow face mask
 HR = heart rate
 LOS = length of stay
 NIV = noninvasive ventilation
 Rx = treatment

beneficial. HFNC reduces the rate of ARF development, re-intubation, and ICU LOS. However, the routine use of HFNC in patients at low risk must be questioned. Based on the 2 studies by Hernández et al,^{87,88} every patient extubated in the ICU would require HFNC, which is clear if Table 9 is examined. All the subjects were divided into either low risk or high risk for re-intubation, and the re-intubation rate in the Hernández et al⁸⁸ low-risk standard oxygen therapy group was very high (12.2%), much higher than would be expected in a low-risk group of patients in a general ICU. Patients identified as low risk for re-intubation in most ICUs have a very low rate, typically <5%, while only receiving standard oxygen therapy.

Summary

A recent meta-analysis by Ni et al⁹⁰ of the use of HFNC after extubation determined that HFNC is superior to standard oxygen therapy in preventing re-intubation but not

superior to NIV. They also determined that HFNC was no better than either standard oxygen therapy or NIV in reducing mortality or LOS in the ICU.⁹⁰ Unfortunately, their analysis did not stratify subjects by risk for re-intubation. Helviz and Einav,⁴ in a recent review of HFNC in adults, indicated that HFNC reduces re-intubation and mortality as much as NIV postextubation in subjects at high risk. But HFNC has not been shown to be beneficial in abdominal surgery subjects and its use in patients at low risk after extubation is controversial. In a recent editorial regarding the use of HFNC postextubation, Mauri et al⁹¹ indicate that HFNC should be limited to patients at risk for re-intubation. Similar results are found in systematic reviews^{3,55} and meta-analysis¹⁵ of the use of NIV and CPAP postextubation. The data are positive in supporting the use of these therapies in the management of patients at high risk of postextubation failure but not for those at low risk of re-intubation. The European Respiratory Society/American Thoracic Society clinical practice guidelines⁵⁶ recommends the use of NIV and/or CPAP for patients with post-operative ARF. No guidelines recommend the use of any of these therapies in patients at low risk of re-intubation.

As outlined in Table 10, currently, there are insufficient data to support the use of NIV, CPAP, or HFNC in the management of patients at low risk of needing re-intubation. However, there is universal support for the use of NIV, CPAP, or HFNC for patients at high risk of requiring re-intubation or patients who develop ARF after extubation. The specific circumstances in which each therapy should be used is unclear.

HFNC has the distinct advantage over NIV and CPAP of being more comfortable and least likely to fail because of patient tolerance, but it should not be the choice of therapy when specific and high levels of PEEP are required or when ventilation is needed. CPAP and HFNC have been advocated for the treatment of hypoxemic respiratory failure; however, if the failure is a result of atelectasis, then CPAP is again the therapy of choice because PEEP is indicated and can be applied at a precise level. This is most likely the reason why HFNC has not

Table 9. Criteria Used to Separate Subjects Into High Risk and Low Risk for Re-Intubation

| Mechanical Ventilation for at Least 12 h and at Least One of the Following | Low Risk | High Risk |
|--|------------|-----------|
| Age 65 y | ≤ | > |
| APACHE II score of 12 at extubation | ≤ | > |
| BMI 30 kg/m ₂ | ≤ | > |
| Pulmonary Secretions | No problem | Problem |
| Comorbidities | ≤1 | >1 |
| HF cause for mechanical ventilation | No | Yes |
| Moderate-severe COPD | No | Yes |
| Airway patency | No problem | Problem |
| Duration of mechanical ventilation | ≤7 d | >7 d |

Based on References 87 and 88.
 APACHE = Acute Physiology and Chronic Health Evaluation
 BMI = body mass index
 HF = heart failure

Table 10. Postextubation Recommendations for the Use of HFNC, NIV, and CPAP

| Parameter | Recommendation |
|--|-------------------------------------|
| Patients at low risk for re-intubation | No indication for HFNC, NIV or CPAP |
| Patients at high risk for re-intubation | HFNC, NIV, and CPAP all indicated |
| Patients who need ventilatory assistance | NIV indicated |
| Patients who require high and precise CPAP levels because of hypoxemic respiratory failure (obese, abdominal surgery, significant atelectasis) | CPAP indicated |
| Patients with hypoxemic respiratory failure who do not require high or precise CPAP levels | HFNC indicated |

HFNC = high-flow nasal cannula
 NIV = noninvasive ventilation

proved to be beneficial in subjects with upper-abdominal surgery or subjects who are obese when high levels of CPAP are required to stabilize the lung. Patients who are hypercarbic require ventilation, hence NIV is indicated. In patients with hypoxemia who require either CPAP or HFNC, the choice is dependent on the need for precise and high PEEP levels. If precise and high PEEP is not needed, then HFNC is the choice.

All 3 therapies have a failure rate that requires intubation. The most difficult task of the bedside clinician is determining when the therapy has failed and when to intubate. As dramatically shown by Esteban et al,⁴⁰ delaying intubation in patients who are not responding positively to any of these therapies leads to increased mortality, most likely caused by the induction of lung injury by vigorous ventilatory efforts.^{43,44} We should always error on the conservative side, and any patient who does not respond to therapy within 1 to 2 h should be intubated. Specifically, patients whose clinical status has not improved, demonstrated by the continual presence of tachypnea, tachycardia, hypotension, or hypertension, and the use of accessory muscles of ventilation in spite of a normalization of blood gases, should be intubated.

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Discussion

*** Hess:** I think that one category of patients (and patients who are obese fall into this group) who get into trouble after extubation are patients who have unrecognized sleep-disordered breathing. Maybe what we're really

treating with NIV is their undiagnosed obstructive sleep apnea.

Kacmarek: I agree. If you look at the history of these patients, you'll find that many of them get extubated and nobody realizes (because they haven't carefully read the history)

that they do have sleep apnea or other forms of sleep disorders that would necessitate some type of therapy after extubation, whether they're obese or lean.

*** Hess:** Right, so we might want to consider adding to the list of people

who are at risk, in addition to history of pulmonary disease and congestive heart failure, is a patient who may have obstructive sleep apnea.

Kacmarek: In the studies that have been done that has not been included as criteria and I extracted right from the criteria of the studies, but I agree with you 100%.

* **Hess:** That's my point. I don't think it was considered.

Kacmarek: It's just like the obese population, very few subjects in any randomized controlled trial are obese. I presented that one study¹ early on with HFNC in subjects after cardiac surgery and with a body mass index $> 30 \text{ kg/m}^2$, but that's the unusual study, it's hard to find studies that look at the obese population.

Hill: Bob [Kacmarek], you've done a very nice job of summarizing what is a very complicated collection of articles in the literature. One of the big challenges, of course, is that we have so many different ways of using noninvasive techniques in the postextubation period; we're using it prophylactically in patients at low risk, or at high risk, or after they've developed frank respiratory failure. We can use it earlier or later, and, in different patient populations, depending on the cause of respiratory compromise. This problem is compounded in the postoperative setting in which your pie chart showed many different types of surgery but very few studies relevant to a single type. Yet, we try to generalize about the whole category of postoperative use. It really does make it difficult to analyze. One of the studies I wanted to comment on specifically was the low-risk study by Hernández et al.²

The intubation rate they observed in their control group was 12%, which is hardly a low-risk group in my view, and many of the subjects were postoperative or had neurologic problems. Is that correct?

Kacmarek: Correct.

Hill: I think it gets at the issue of what kinds of patients you include in your study population. If you have people with potential swallowing or secretion problems, as the subjects in the study by Hernández et al.² probably had, then HFNC may be helpful. However, a more typical low-risk postextubation population probably wouldn't manifest a difference in intubation rate because the control rate would likely be considerably lower than in the Hernández's study.

Kacmarek: Right, if you go to your standard surgical ICU and you use the 2 categories low risk and high risk, that's everybody. In our ICU, that is, every patient we extubate would need to go on HFNC, and I clearly don't believe that's the case. I think we need better studies. On the high-risk side, I don't think any of us would question the need for some type of noninvasive support, but, on the low-risk side, I don't think we've teased out the correct subgroups who would benefit from HFNC.

Hill: The study by Ferrer et al.³ on subjects who were hypercapnic, the thing that disturbed me about that study was that the main difference they showed was in the rate of respiratory failure, which they defined as exceeding a certain level of hypercapnia. So you randomize them to go on NIV or standard oxygen, and it makes sense that NIV would prevent greater hypercapnia, thus preventing respiratory failure as they defined it. Also, based on what we know now about the overuse of O_2

in patients with COPD and who are hypercapnic, you could create a situation in which just by virtue of the aggressiveness of your oxygenation . . .

Kacmarek: You create a problem. Yeah, I agree, this was not the best study. To me, this was a little confusing because I didn't think the criteria for fitting the ARF definition was as clear as it could have been.

Hill: Even though I agree with the conclusion that NIV is helpful when people are hypercapnic and are at risk of going into respiratory failure, I'm not sure this was the best way to demonstrate it.

Volsko: With regard to the neonatal data that you presented for HFNC, what was the approach the investigators took with setting the flow? In early use of HFNC in practice, there was some hesitancy to use the higher flows because the CPAP level was thought to be highly variable.⁴

Kacmarek: If you look at the top group in which they looked at failure,⁵ the first study included was from 2011. So there was only one older study that they included in the criteria when selecting the particular studies included in the meta-analysis. I agree, the flows early on were all over the place and nothing was standardized, but I think the majority of the studies are recent enough that they reflect standard care in our neonatal ICU.

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