Non-invasive
Increase flow rate-match patient rate
Increase $O_2$ delivery
Compared with NIV /conventional $O_2$

In next few minutes

- Evidence
- Rationale
- ? Any harm
- Balanced approach
54 male
HT, DM
CAP, HFO2, RR25, Fio2 70
6 hours of treatment
12 hours of treatment
24 hours of treatment
48 hours of treatment
72 hours of treatment
Immunocompromised
84 year old
84 year old with multiple comorbidity
Medical-Hypoxic RF

ICU/ED Immunocompromised Palliation

➢ > Stand O₂
➢ Non inferior to NIV

<table>
<thead>
<tr>
<th>Study</th>
<th>Design/N</th>
<th>Patients</th>
<th>Comparison</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prevention of reintubation after cardiac surgery</td>
<td>Corley and colleagues, 2015 (59) RCT 155</td>
<td>BMI ≥30 kg/m²</td>
<td>HFNC 35-50 L/min vs. COT</td>
<td>No difference in PaO₂/FiO₂ after 24 h</td>
</tr>
<tr>
<td>Parke and colleagues, 2013 (58) RCT 340</td>
<td>Not stratified by reintubation risk</td>
<td>HFNC 45 L/min vs. usual care</td>
<td>No difference in atelectasis by Day 5</td>
<td></td>
</tr>
<tr>
<td>Parke and colleagues, 2011 (60) RCT 60</td>
<td>Surgical ICU Most were post-cardiac surgery</td>
<td>HFNC 35 L/min vs. COT</td>
<td>Fewer in HFNC group required escalation of respiratory support</td>
<td></td>
</tr>
<tr>
<td>Stephan and colleagues, 2015 (57) RCT 830</td>
<td>Previously failed extubation or high risk for reintubation</td>
<td>HFNC 50 L/min vs. NIV</td>
<td>Lower NIV use with HFNC (10%) vs. COT (30%)</td>
<td></td>
</tr>
<tr>
<td>Prevention of reintubation after abdominal surgery</td>
<td>Futier and colleagues, 2016 (61) RCT 220</td>
<td>High risk for reintubation</td>
<td>Fewer desaturation events with HFNC</td>
<td></td>
</tr>
<tr>
<td>Thoracic surgery</td>
<td>Ansari and colleagues, 2016 (64) RCT 59</td>
<td>Post-lung resection</td>
<td>No difference in reintubations or ICU mortality</td>
<td></td>
</tr>
<tr>
<td>Yu and colleagues, 2017 (63) RCT</td>
<td>Post lobectomy High risk for reintubation</td>
<td>HFNC 35-60 L/min vs. COT</td>
<td>More skin breakdown with NIV</td>
<td></td>
</tr>
</tbody>
</table>
### Apnoeic oxygenation

**Bronchoscopy**

<table>
<thead>
<tr>
<th>Study</th>
<th>Design/N</th>
<th>Patients</th>
<th>Comparison</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preoxygenation and apnoeic oxygenation for intubation</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Jaber and colleagues, 2016 (67)</td>
<td>RCT</td>
<td>RR &gt;30 breaths/min, FIO₂ &gt; 50%</td>
<td>Preoxygenation with HFNC 60 L/min + NIV vs. NIV alone</td>
<td>HFNC + NIV combination improved oxygenation vs. NIV alone</td>
</tr>
<tr>
<td></td>
<td></td>
<td>PaO₂/FIO₂ &lt; 300 requiring MV</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Miguel-Montanes, and colleagues, 2015 (71)</td>
<td>Before-after</td>
<td>All patients requiring MV</td>
<td>Before: NRB After: HFNC 60 L/min</td>
<td>HFNC reduced severe hypoxemia (SpO₂ &lt; 80%)</td>
</tr>
<tr>
<td>Semler and colleagues, 2016 (70)</td>
<td>RCT</td>
<td>All patients requiring MV</td>
<td>HFNC 15 L/min during laryngoscopy vs. no oxygen</td>
<td>No difference in hypoxemia</td>
</tr>
<tr>
<td>Simon and colleagues, 2016 (69)</td>
<td>RCT</td>
<td>PaO₂/FIO₂ &lt; 300 requiring MV</td>
<td>HFNC 50 L/min before/during laryngoscopy vs. bag mask before</td>
<td>No difference in hypoxemia</td>
</tr>
<tr>
<td>Vourch and colleagues, 2015 (68)</td>
<td>RCT</td>
<td>RR &gt;30 breaths/min, FIO₂ &gt;50%, PaO₂/FIO₂ &lt;300 requiring MV</td>
<td>HFNC 60 L/min before/during laryngoscopy vs. face mask before</td>
<td>No difference in hypoxemia</td>
</tr>
<tr>
<td>Bonechoscopy</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lucangelo and colleagues, 2012 (75)</td>
<td>RCT</td>
<td>Diagnostic bronchoscopy</td>
<td>HFNC 40 L/min, HFNC 60 L/min, or Venturi mask 40 L/min</td>
<td>60 L/min HFNC improved hypoxemia and PaO₂/FIO₂ ratio better than 40 L/min HFNC and Venturi mask</td>
</tr>
<tr>
<td></td>
<td></td>
<td>No respiratory or cardiac failure</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Simon and colleagues, 2014 (76)</td>
<td>RCT</td>
<td>Diagnostic bronchoscopy</td>
<td>HFNC 50 L/min vs. NIV</td>
<td>Similar oxygenation during procedure</td>
</tr>
<tr>
<td></td>
<td></td>
<td>PaO₂/FIO₂ &lt; 300</td>
<td></td>
<td>One HFNC, three NIV required intubation within 24 h</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Approximately three-fourths of patients were on NIV or HFNC at baseline</td>
</tr>
</tbody>
</table>
Summary

- 13 Meta-analysis
- >40 expert opinions/ reviews/ editorial
- 16 studies
  - 7- HFO\textsubscript{2} No better than Conv O\textsubscript{2} / NIV
  - 5- HFO\textsubscript{2}>Conv O\textsubscript{2} but not NIV
  - 1- HFO\textsubscript{2}> Conv O\textsubscript{2} / NIV
FLORALI study

- **Intervention**
  - Mask - 10l/min
  - NIV - 9 ml/kg
  - HFO2 - 50 l/MT

- **Inclusion**
  - Adult RR > 25
  - PF < 300
  - PaCO$_2$ < 45

- **Exclusion**
  - COPD
  - HF
  - HD instability
  - Altered conscious state

Primary outcome - proportion of patients who required endotracheal intubation within 28 days after randomization

Primary outcome

- Rate of intubation
  - 38% HFNC
  - 47% Stan O₂
  - 50% NIV

Assumption: reduction in intubation from 60 to 40%
Subgroup analysis

B. Patients with a $\text{PaO}_2:\text{FiO}_2 \leq 200$ mm Hg

- Noninvasive ventilation
- Standard oxygen
- High-flow oxygen

Cumulative Incidence of Intubation

Days since Enrollment

$P=0.009$ by log-rank test

No. at Risk

<table>
<thead>
<tr>
<th></th>
<th>83</th>
<th>55</th>
<th>54</th>
<th>54</th>
<th>53</th>
<th>53</th>
<th>53</th>
<th>53</th>
</tr>
</thead>
<tbody>
<tr>
<td>High-flow oxygen</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Standard oxygen</td>
<td>74</td>
<td>37</td>
<td>35</td>
<td>34</td>
<td>34</td>
<td>34</td>
<td>33</td>
<td>33</td>
</tr>
<tr>
<td>Noninvasive ventilation</td>
<td>81</td>
<td>41</td>
<td>34</td>
<td>32</td>
<td>32</td>
<td>32</td>
<td>32</td>
<td>32</td>
</tr>
</tbody>
</table>
### Table 2. (Continued.)

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Study Group</th>
<th>P Value↑</th>
<th>Odds Ratio or Hazard Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>In ICU</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unadjusted analysis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of patients</td>
<td>12</td>
<td>18</td>
<td>27</td>
</tr>
<tr>
<td>% of patients (95% CI)</td>
<td>11 (6–19)</td>
<td>19 (12–28)</td>
<td>25 (17–33)</td>
</tr>
<tr>
<td>Adjusted analysis**</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>At day 90</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall population</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unadjusted analysis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of patients</td>
<td>13</td>
<td>22</td>
<td>31</td>
</tr>
<tr>
<td>% of patients (95% CI)</td>
<td>12 (7–20)</td>
<td>23 (16–33)</td>
<td>28 (21–37)</td>
</tr>
<tr>
<td>Adjusted analysis**</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intubated patients</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of patients/total. no.</td>
<td>12/40</td>
<td>20/44</td>
<td>27/55</td>
</tr>
<tr>
<td>% of patients (95% CI)</td>
<td>30 (18–46)</td>
<td>45 (32–60)</td>
<td>49 (36–62)</td>
</tr>
</tbody>
</table>
Important consideration

- NHFO$_2$ > NIV interruptions

Dec dead space by 60 ml

10 l/min flow rate = 1 cm PEEP

Delivery of inspired gas at 30 degrees C, or even 34 degrees C, with 100% RH may not be sufficient to prevent epithelial damage occurring during 6 h exposure.

20% cell death

HFNC was better tolerated and more comfortable than face mask.

HFNC was associated with better oxygenation and lower respiratory rate.

In patients with AHRF, HFNC exerts multiple physiologic effects including less inspiratory effort and improved lung volume and compliance

Not everyone benefited

- 42% mortality if intubated
- 4% mortality if not intubated
- **Cause of death**
  - Refractory shock – 54%
  - Hypoxemia – 29%
  - Cardiac arrest – 8%

- Intubation delay
- NIV: Ventilator induced lung injury (VILI)
- HFO2: Patient self induced lung injury (pSILI)
- High Fio2 – Respiratory epithelial injury
- High Oxygenation – oxidation injury

Not MOF
Respiratory response to CO$_2$

- RR – measured
- TV - Not measured

Experimental evidence

Experimental evidence

Dreaded fibrosis


**Figure 3.** Bronchoalveolar lavage fluid and serum N-PCP-III concentrations at 24 h. N-PCP-III concentrations were determined by radioimmunoassay in BALF and serum samples obtained within 24 h of diagnosis. Each point represents the average of duplicate determinations for an individual patient. Bars represent median values.
Direct evidence of harm

Failure of HFNC might cause delayed intubation and worse clinical outcomes in patients with respiratory failure.

- May delay intubation
  - Failure MR 40 to 50%
- May contribute to lung injury
  - Self inflicted lung injury
- pSILI vs whole body harm – intubation
### TABLE 3. Multivariate Logistic Regression Analyses of Factors Associated With Intubation

<table>
<thead>
<tr>
<th>Risk Factors</th>
<th>OR (95% CI)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>In patients treated with conventional O$_2$ therapy by nonbreathing mask$^a$</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Respiratory rate $\geq$ 30 breaths/min at H1</td>
<td>2.76 (1.13–6.75)</td>
<td>0.03</td>
</tr>
<tr>
<td>In patients treated with high-flow nasal cannula oxygen therapy$^a$</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heart rate at H1 (per beat/min)</td>
<td>1.03 (1.01–1.06)</td>
<td>$&lt;0.01$</td>
</tr>
<tr>
<td>In patients treated with noninvasive ventilation$^{ab}$</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tidal volume $\geq$ 9mL/kg of predicted body weight at H1</td>
<td>3.14 (1.22–8.06)</td>
<td>0.02</td>
</tr>
<tr>
<td>Pao$_2$/FiO$_2$ $\leq$ 200 mm Hg at H1</td>
<td>4.26 (1.62–11.16)</td>
<td>0.003</td>
</tr>
</tbody>
</table>

---

Prediction - ROX index

- 4-year prospective observational 2-center cohort study
- Patients with severe pneumonia treated with HFNC
- ROX index was defined as the ratio of pulse oximetry/fraction of inspired oxygen to respiratory rate
- After 12 hours ROX index demonstrated the best prediction accuracy - AUC -0.74

Special consideration

- May facilitate intubation
- May delay diagnostic testing
- HF with pneumonia
- OSA with pneumonia
Summary of evidence (again)

- 13 Meta-analysis
- >40 expert opinions/ reviews/ editorial
- 16 studies
  - 7- HFO\textsubscript{2} No better than Conv O\textsubscript{2} /NIV
  - 5- HFO\textsubscript{2}> Conv O\textsubscript{2} but not NIV
  - 1- HFO\textsubscript{2}> CONV O\textsubscript{2}/NIV
Non inferior to NIV
NIV not recommended
So same principles as ERJ 2017
“Given the uncertainty of evidence we are unable to offer a recommendation on use of NIV for denovo ARF”
NIV and lung injury

- Lung SAFE
- PF<150 NIV vs intubation

Considered that some studies have shown some benefit

• “Use only if
  • Experienced clinical team
  • No contraindications
  • Carefully selected
  • Close monitoring in ICU
  • Reassessed frequently and early
  • Intubated promptly if not improving”

Same principles apply to NHO₂

Rochwerg ERJ 2017
54 male
HT, DM
CAP, HFO2, RR25, Fio2 60
6 hours of treatment
12 hours of treatment
24 hours of treatment
48 hours of treatment
72 hours of treatment
Immuno compromised
84 year old
84 year old with multiple comorbidity
Conclusion

- AHRF- NHO$_2$ prevents re intubation after extubation - standard oxygen therapy
- AHRF- non inferior to NIV
- Denovo AHRF- high proportion of patients with require intubation - NHFO$_2$
- Delayed intubation with NHO$_2$ – SILI- increased ICU mortality
- Reinforces the need of an appropriate environment and team

Bihari S, Bersten AD. High-flow nasal cannula oxygen therapy in acute hypoxemic respiratory failure: Proceed with caution. CMAJ. 2017 Feb 21;189(7):E258-E259
Future

- Better prediction tools / monitoring
  - WOB/ Resp drive
  - Diaphragm excursion / thickening
- Safer way to deliver HFo2
  - Helmet with nHFO₂
    - HFNC, flow is set, and pressure is variable, while with HELMET CPAP, pressure is set and flow is variable
    - Advantage - stable PEEP, effective CO₂ washout

*Nasal High Flow Delivered within the Helmet: A New Non-Invasive Respiratory Support.* American Journal of Respiratory and Critical Care Medicine
ERS / ATS

- NIV for ARF
- Hypoxemia PF<200
- Tachypnea 30-35
- Non COPD- Pneumonia / ARDS
Given the uncertainty of evidence we are unable to offer a recommendation on use of NIV for denovo ARF

So if it was a drug it will not receive FDA approval for this indication

Rochworg ERJ 2017
Indications

- Increase O2 requirement
- Increase WOB
- Prevent complications with intubations and IMV
Delayed intubation

- High MR – Kang ICM 2015
- No predictor of failure in NHFO2
- Delaying diagnostic procedure with nasal HFO2
- However, communication better
- How to proceed in non-responders
how to predict

- NIV
  - VT > 9 ml/kg
  - p/f < 200
  - RR > 30 on stand O2

- But nhfo2 predictors not available
May facilitate intubation in resp failure


Patient preference

- HF with pneumonia
- OSA with pneumonia
- Diaphragm WOB
14 MA can HF nasal cannula reduce ...


- Sto2 RR
- HFO2
ARDS/AHRF

- Could be UL
- Not intubated – not on PEEP
OBJECTIVE  To determine whether high-flow nasal oxygen therapy was not inferior to BiPAP for preventing or resolving acute respiratory failure after cardiothoracic surgery.

DESIGN AND SETTING  Multicenter, randomized, noninferiority trial (BiPAP Study) conducted between June 15, 2011, and January 15, 2014, at 6 French intensive care units.

PARTICIPANTS  A total of 830 patients who had undergone cardiothoracic surgery, of which coronary artery bypass, valvular repair, and pulmonary thromboendarterectomy were the most common, were included when they developed acute respiratory failure (failure of a spontaneous breathing trial or successful breathing trial but failed extubation) or were deemed at risk for respiratory failure after extubation due to preexisting risk factors.

INTERVENTIONS  Patients were randomly assigned to receive high-flow nasal oxygen therapy delivered continuously through a nasal cannula (flow, 50 L/min; fraction of inspired oxygen [FIO2] 50%) (n = 414) or BiPAP delivered with a full-face mask for at least 4 hours per day (pressure support level, 8 cm H2O; positive end-expiratory pressure, 4 cm H2O; FIO2 50%) (n = 416).

MAIN OUTCOMES AND MEASURES  The primary outcome was treatment failure, defined as reintubation, switch to the other study treatment, or premature treatment discontinuation (patient request or adverse effects, including gastric distention). Noninferiority of high-flow nasal oxygen therapy would be demonstrated if the lower boundary of the 95% CI were less than 5%. Secondary outcomes included mortality during intensive care unit stay, changes in respiratory variables, and respiratory complications.

RESULTS  High-flow nasal oxygen therapy was not inferior to BiPAP: the treatment failed in 87 of 414 patients with high-flow nasal oxygen therapy (21.0%) and 91 of 416 patients with BiPAP (21.9%) (absolute difference, 0.9%; 95% CI, –4.9% to 6.6%; P = .003). No significant differences were found for intensive care unit mortality (23 patients with BiPAP [5.5%] and 28 with high-flow nasal oxygen therapy [6.8%]; P = .66) (absolute difference, 1.2%; 95% CI, –2.3% to 4.8%). SkoI breakdown was significantly more common with BiPAP after 24 hours (10% vs 3%; 95% CI, 7.3%–13.4% vs 1.8%–5.6%; P < .001).

CONCLUSIONS AND RELEVANCE  Among cardiothoracic surgery patients with or at risk for respiratory failure, the use of high-flow nasal oxygen therapy compared with intermittent BiPAP did not result in a worse rate of treatment failure. The findings support the use of high-flow nasal oxygen therapy in similar patients.

TRIAL REGISTRATION  clinicaltrials.gov Identifier NCT01456444

Published online May 17, 2016.

Author Affiliations: Author affiliations are listed at the end of this article.

Group Information: The BiPAP Study Group members are listed at the end of this article.

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Section Editor: Derek C. Angus, MD, MPH, Associate Editor, JAMA (angusc@upmc.edu).
High-flow nasal cannula oxygen versus non-invasive ventilation in patients with acute hypoxaemic respiratory failure undergoing flexible bronchoscopy - a prospective randomised trial

Marcel Simon1, Stephan Braune1, Daniel Frings1, Ann-Kathrin Wöntzek1, Hans Klose1 and Stefan Kluge1

Abstract

Introduction: Critically ill patients with respiratory failure undergoing bronchoscopy have an increased risk of hypoxaemia-related complications. Previous studies have shown that in awake, hypoxaemic patients non-invasive ventilation (NIV) is helpful in preventing gas exchange deterioration during bronchoscopy. An alternative and increasingly used means of oxygen delivery is high-flow nasal cannula (HFNC). This study was conducted to compare HFNC with NIV in patients with acute hypoxaemic respiratory failure undergoing flexible bronchoscopy.

Methods: Prospective randomised trial randomising 40 critically ill patients with hypoxaemic respiratory failure to receive either NIV or HFNC during bronchoscopy in the intensive care unit.

Results: After the initiation of NIV and HFNC, oxygen levels were significantly higher in the NIV group compared to the HFNC group. Two patients were unable to proceed to bronchoscopy after the institution of HFNC due to progressive hypoxaemia. During bronchoscopy, one patient on HFNC deteriorated due to intravenous sedation requiring non-invasive ventilatory support. Bronchoscopy was well tolerated in all other patients. There were no significant differences between the two groups regarding heart rate, mean arterial pressure and respiratory rate. Three patients in the NIV group and one patient in the HFNC group were intubated within 24 hours after the end of bronchoscopy ($P = 0.29$).

Conclusions: The application of NIV was superior to HFNC with regard to oxygenation before, during and after bronchoscopy in patients with moderate to severe hypoxaemia. In patients with stable oxygenation under HFNC, subsequent bronchoscopy was well tolerated.

Trial registration: ClinicalTrials.gov NCT01870765. Registered 30 May 2013.
High-flow nasal cannula oxygen therapy versus noninvasive ventilation in immunocompromised patients with acute respiratory failure: an observational cohort study

Rémi Coudroy\textsuperscript{1,2*}, Angéline Jarnet\textsuperscript{1}, Philippe Petua\textsuperscript{1}, René Robert\textsuperscript{1,2}, Jean-Pierre Frat\textsuperscript{1,2} and Arnaud W. Thille\textsuperscript{1,2}

Abstract

Background: Acute respiratory failure is the main cause of admission to intensive care unit in immunocompromised patients. In this subset of patients, the beneficial effects of noninvasive ventilation (NIV) as compared to standard oxygen remain debated. High-flow nasal cannula oxygen therapy (HFNC) is an alternative to standard oxygen or NIV, and its use in hypoxemic patients has been growing. Therefore, we aimed to compare outcomes of immunocompromised patients treated using HFNC alone or NIV as a first-line therapy for acute respiratory failure in an observational cohort study over an 8-year period. Patients with acute-on-chronic respiratory failure, those treated with standard oxygen alone or needing immediate intubation, and those with a do-not-intubate order were excluded.

Results: Among the 115 patients analyzed, 60 (52 \%) were treated with HFNC alone and 55 (48 \%) with NIV as first-line therapy with 30 patients (55 \%) receiving HFNC and 25 patients (45 \%) standard oxygen between NIV sessions. The rates of intubation and 28-day mortality were higher in patients treated with NIV than with HFNC (55 vs. 35 \%, \(p = 0.04\), and 40 vs. 20 \%, \(p = 0.02\) log-rank test, respectively). Using propensity score-matched analysis, NIV was associated with mortality. Using multivariate analysis, NIV was independently associated with intubation and mortality.

Conclusions: Based on this observational cohort study including immunocompromised patients admitted to intensive care unit for acute respiratory failure, intubation and mortality rates could be lower in patients treated with HFNC alone than with NIV. The use of NIV remained independently associated with poor outcomes.

Keywords: Acute respiratory failure, Immunosuppression, Noninvasive positive pressure ventilation, Acute lung injury, Mechanical ventilation, High-flow oxygen therapy
Helmet mask – Patel BK
JAMA 2016 315; 2435