Role of High Flow Nasal Cannula in Respiratory Failure

Puneet Saxena

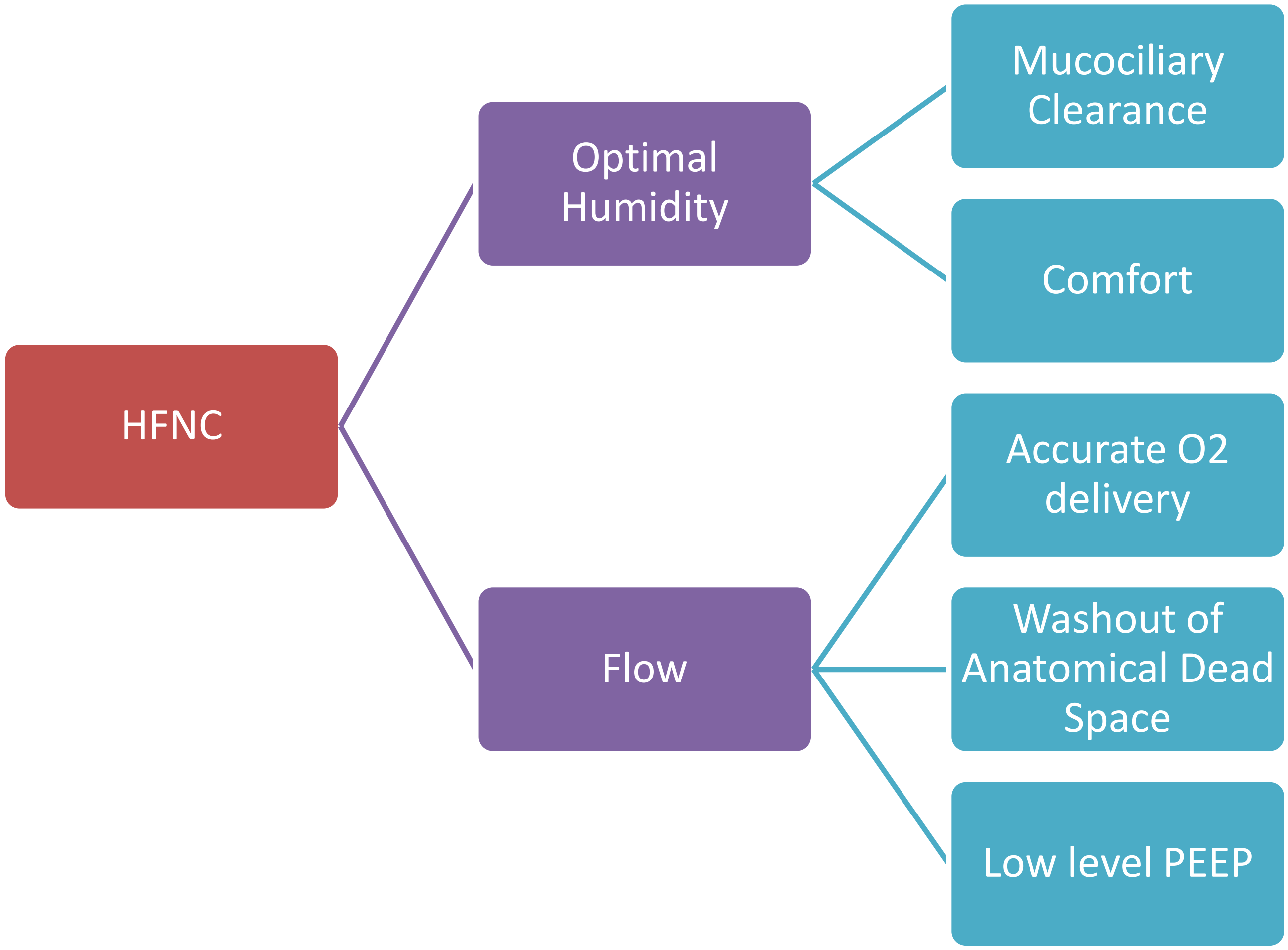
Outline

- Mechanisms and Physiology
- Preliminary studies
- Clinical Uses
  - Acute Hypoxemic Respiratory Failure
  - Immunocompromised patients
  - DNI
  - Before intubation
  - After extubation
  - Post OP
- Emerging evidence
- Uncertainities

Mechanisms and Physiology

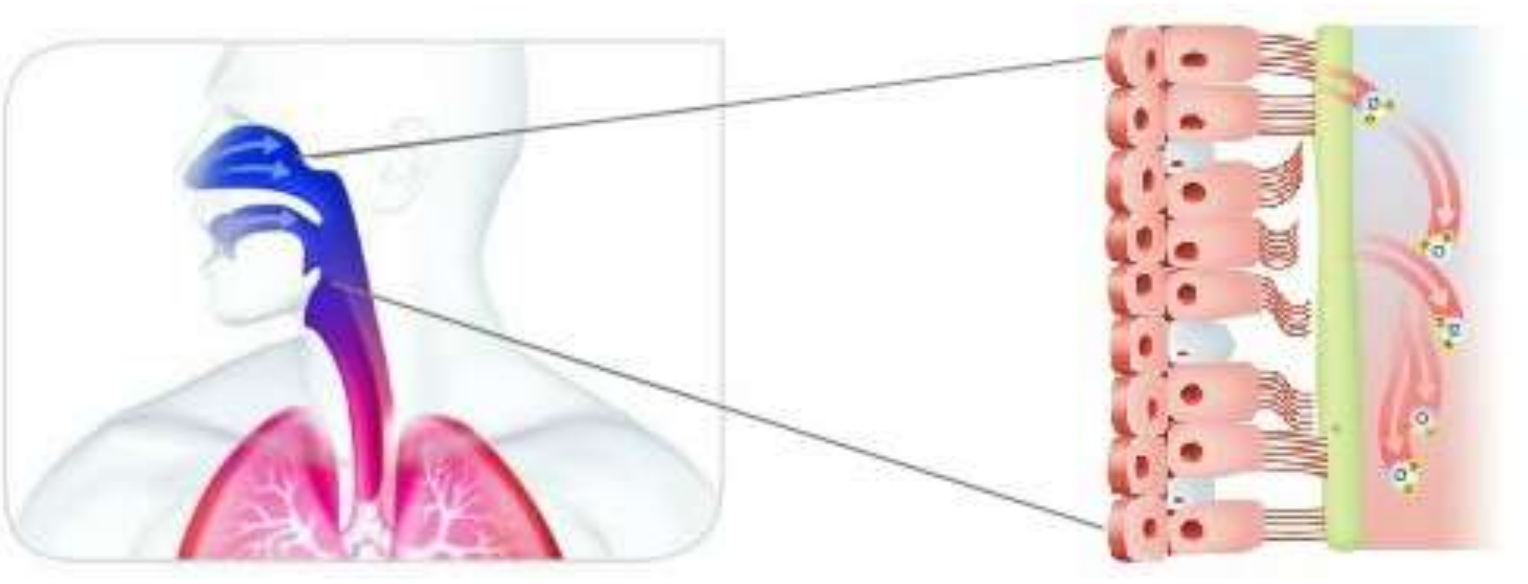
- Conventional oxygen devices provide much lesser flows than inspiratory flow rates
- Higher flows are not tolerated by the patients
  - Warm humid gas is associated with better conductance and pulmonary compliance compared to dry, cooler gas
- Inconsistent FiO2s
- Masks and reservoirs increase the dead space

Key Benefits



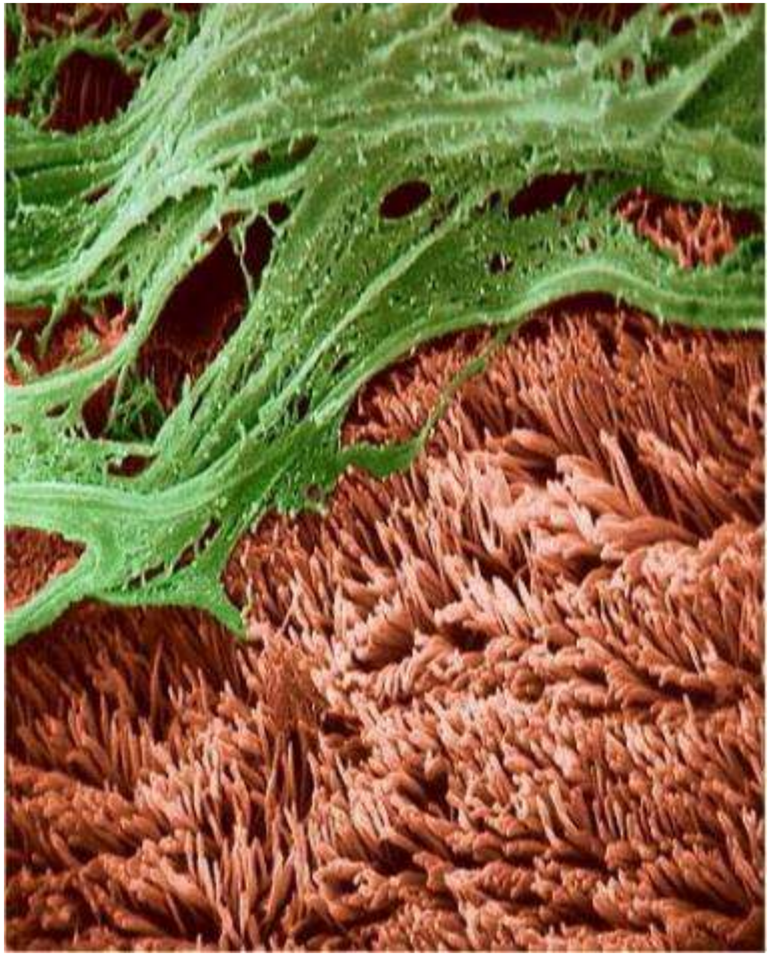
Optimal Humidity

- Optimal Humidity is 37 °C , 44 mg/L, 100% RH:
  - Emulates the natural balance of heat and humidity in healthy human lung
  - Enables the comfortable delivery of high flows



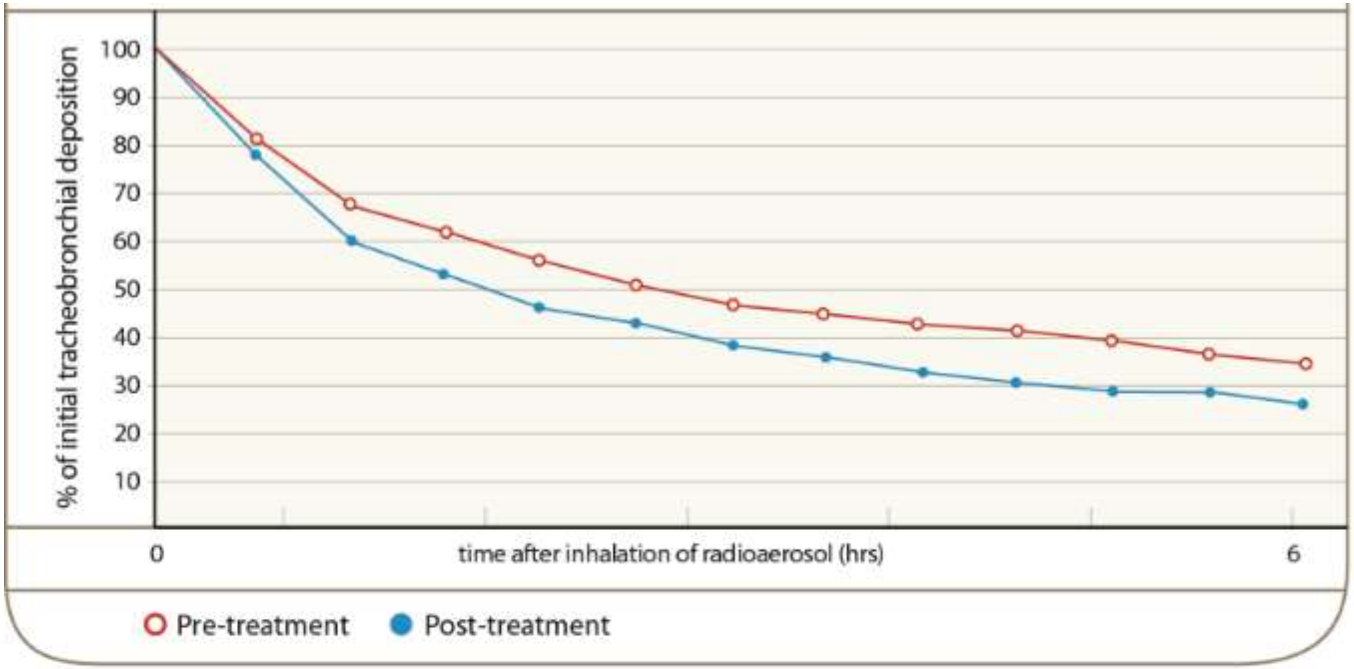
Optimized Mucociliary Clearance

- Delivering Optimal Humidity (37 °C , 44 mg/L) optimizes mucociliary clearance
  - Improves secretion quality
  - Maintains mobility of secretions for transport out of the airway
  - Reduces the risk of respiratory infection



Optimized Mucociliary Clearance

- Radio-aerosol technique to measure mucociliary clearance before and after 7 days of humidification



($p < 0.007$)

Hasani et al. Chron Respir Dis. 2008;5(2):81-6.

Comfort

- AIM
  - To compare the comfort and effectiveness of HFNC; with conventional face mask oxygen therapy in patients with ARF
- ARF was defined as $SPO_2 < 96\%$ while receiving a $FiO_2 > 0.50$ via face mask
- 20 patients with ARF, comparison of 2 periods: 30 mins face mask (humidified with a bubble humidifier) and 30 mins with HFNC
- At the end of each 30-min period patients were asked to evaluate dyspnea, mouth dryness, and overall comfort, on a VAS of 0 (lowest) to 10 (highest)

Roca et al. Respir Care 2010;55(4):408–413

Roca et al. (2010)

	FACE MASK	HFNC	*P*
Dyspnea	6.8	3.8	0.001
Mouth dryness	9.5	5.0	<0.001
Overall comfort	5.0	9.0	<0.001

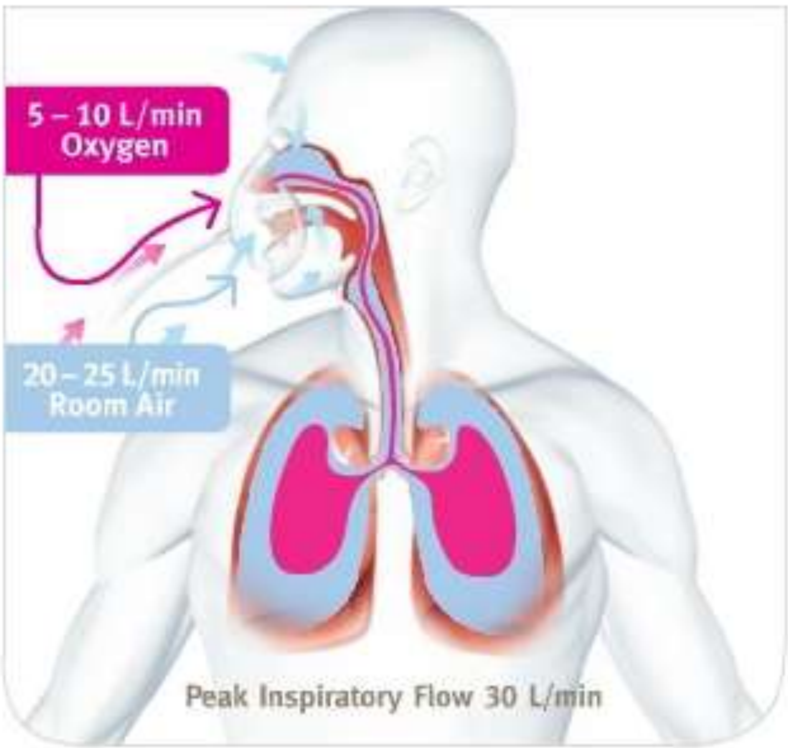
Median of scores recorded on a visual analogue scale ranging from 0 (lowest) to 10 (highest)

- All patients continued with HFNC as their chosen therapy
- Higher PaO_2 (127 mmHg vs 77 mmHg, $P = .002$) and lower respiratory rate (21 b/min vs 28 b/min, $P < .001$), but no difference in $PaCO_2$

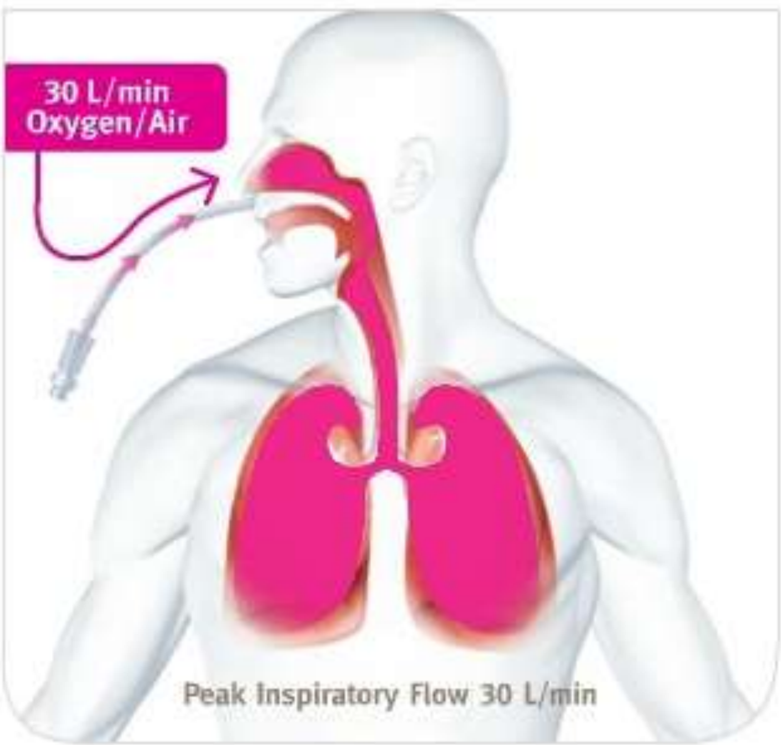
Roca et al. Respir Care 2010;55(4):408–413

Accurate Oxygen Delivery

Face Mask

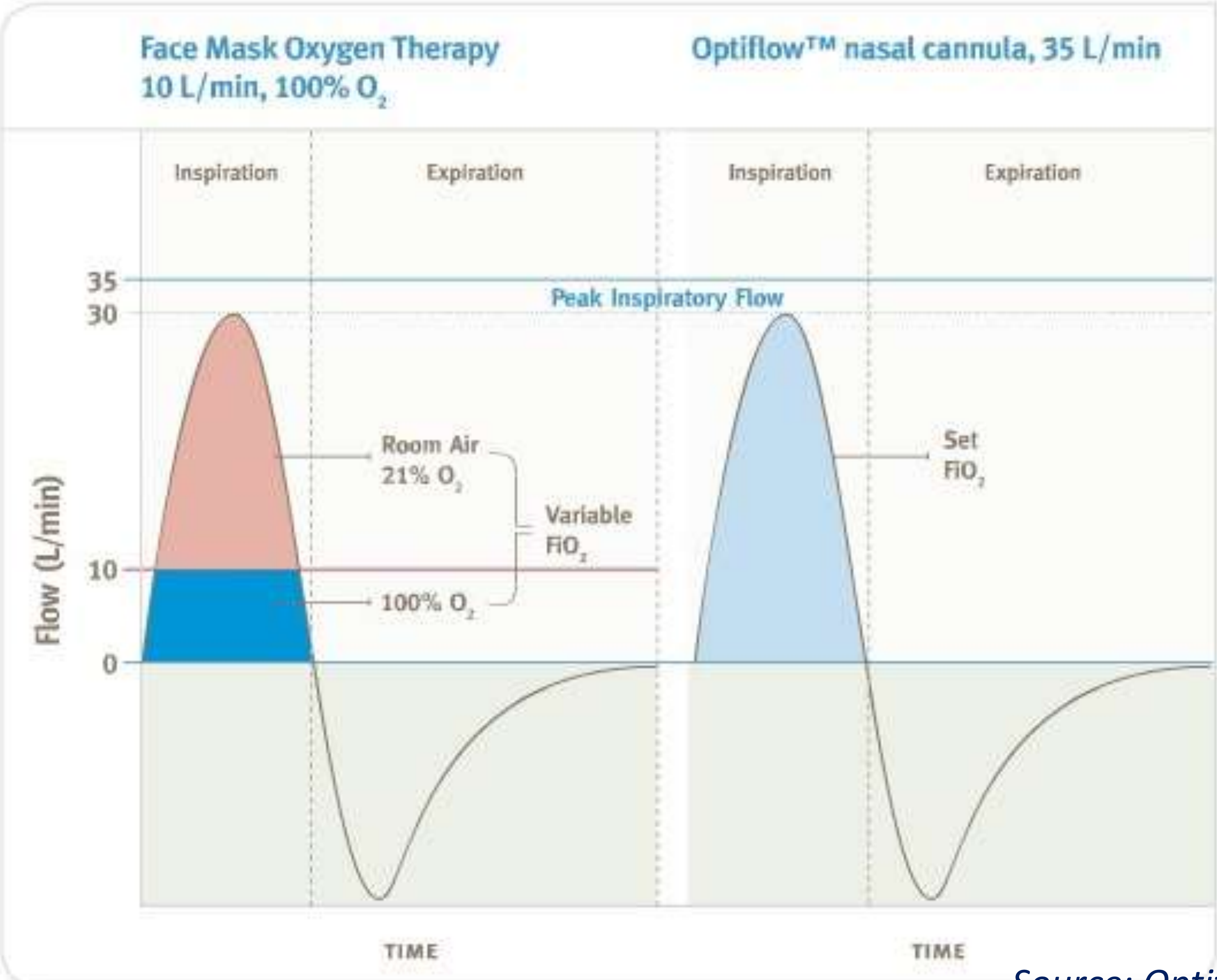


HFNC



Source: Optiflow® - Manual

Accurate Oxygen Delivery



Source: Optiflow® - Manual

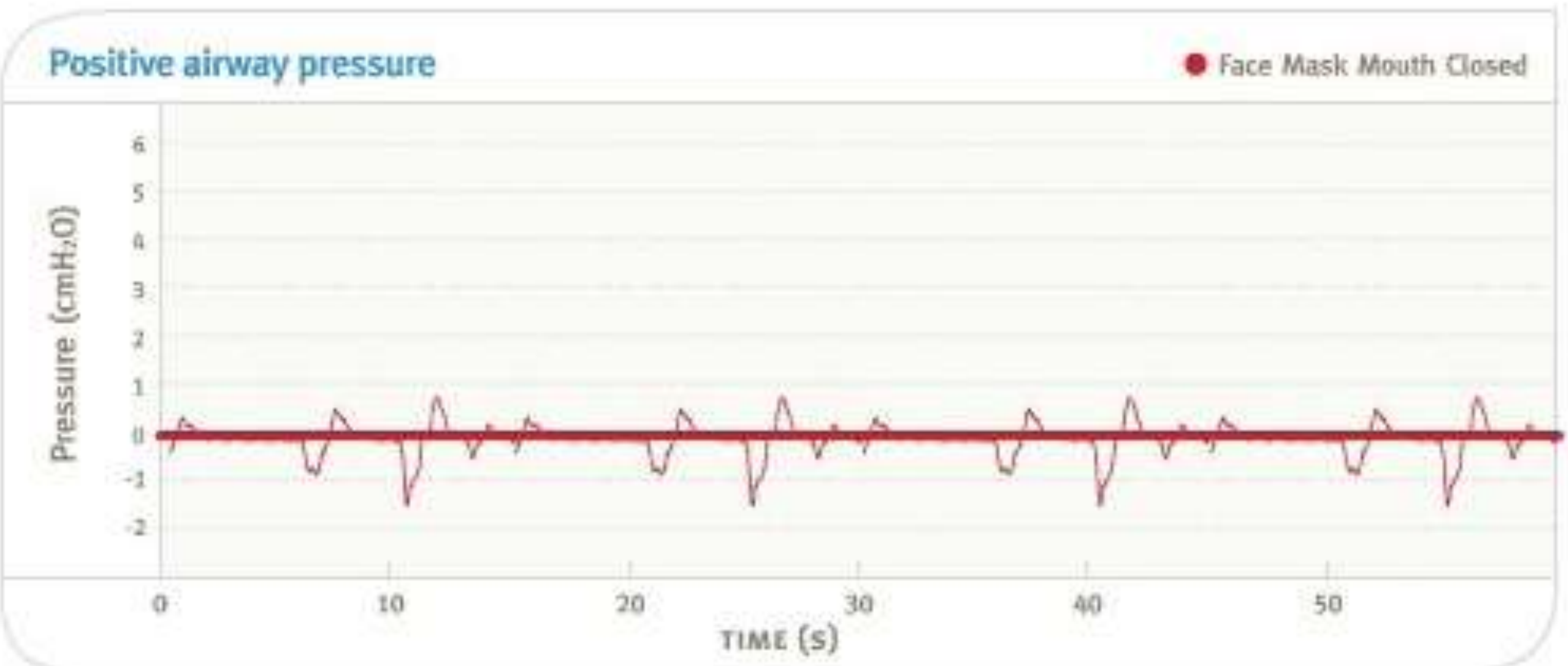
Washout of Anatomical Deadspace

- Washout effect in the pt's anatomical deadspace in the upper airway

- Effect aims to:
  - Reduce re-breathing of expired CO2
  - Create a reservoir of fresh gas in the upper airway, ready for the next inspiration
  - Allow for better ventilation and oxygenation

Low-Level Pressure Delivery

Parke et al. (2009) compared the level of positive airway pressure generated by HFNC with traditional face mask oxygen therapy



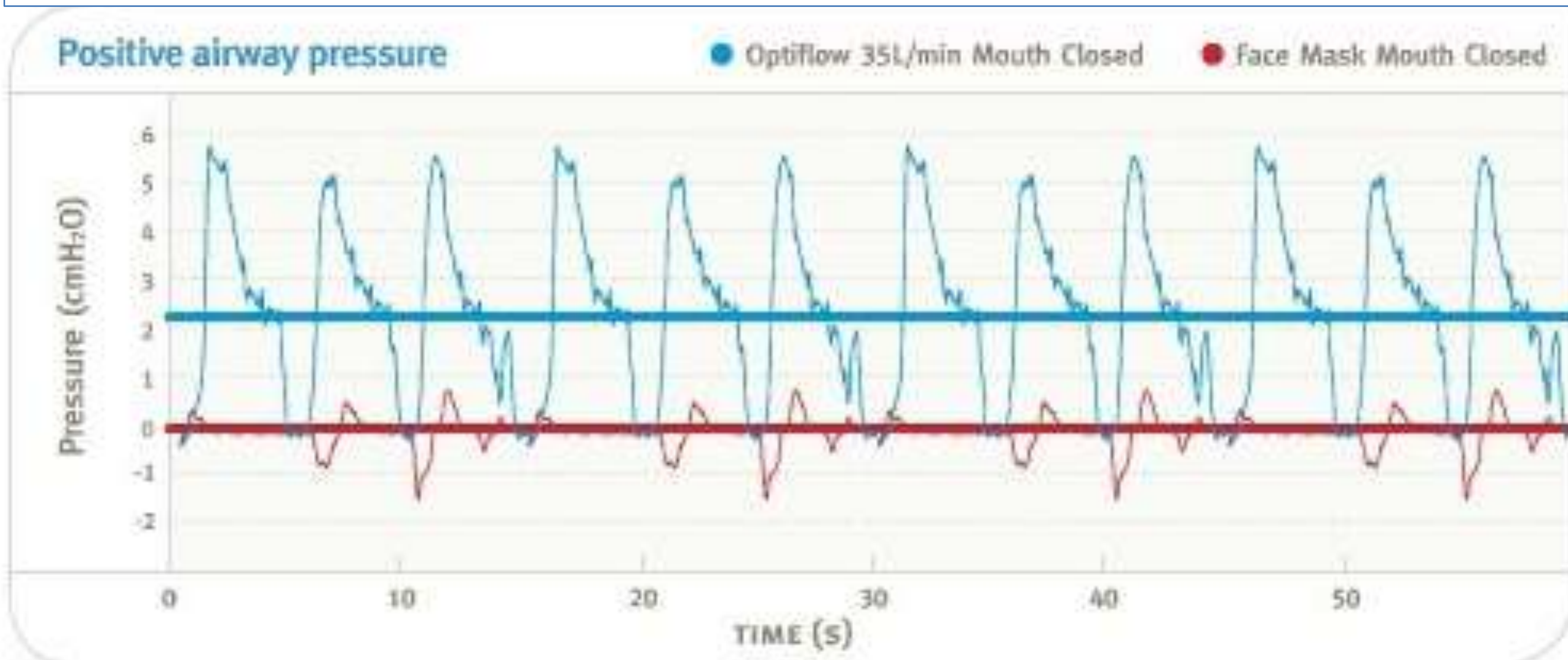
Br J Anaesth 2009; 103: 886–90

Low-Level Pressure Delivery

RESULTS

•The continuous flows of gas delivered into the nares by HFNC generated a low-level pressure

•Mean airway pressure was significantly higher with HFNC ($p < 0.0001$)

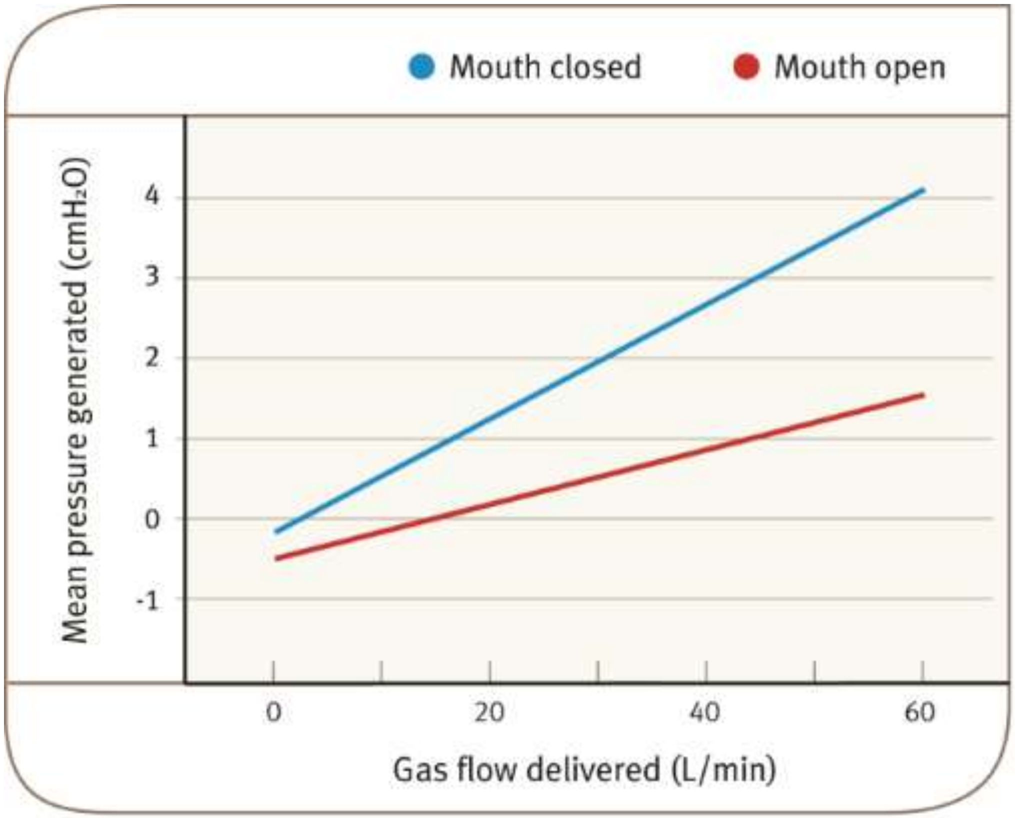


Br J Anaesth 2009; 103: 886–90

Flow vs Pressure

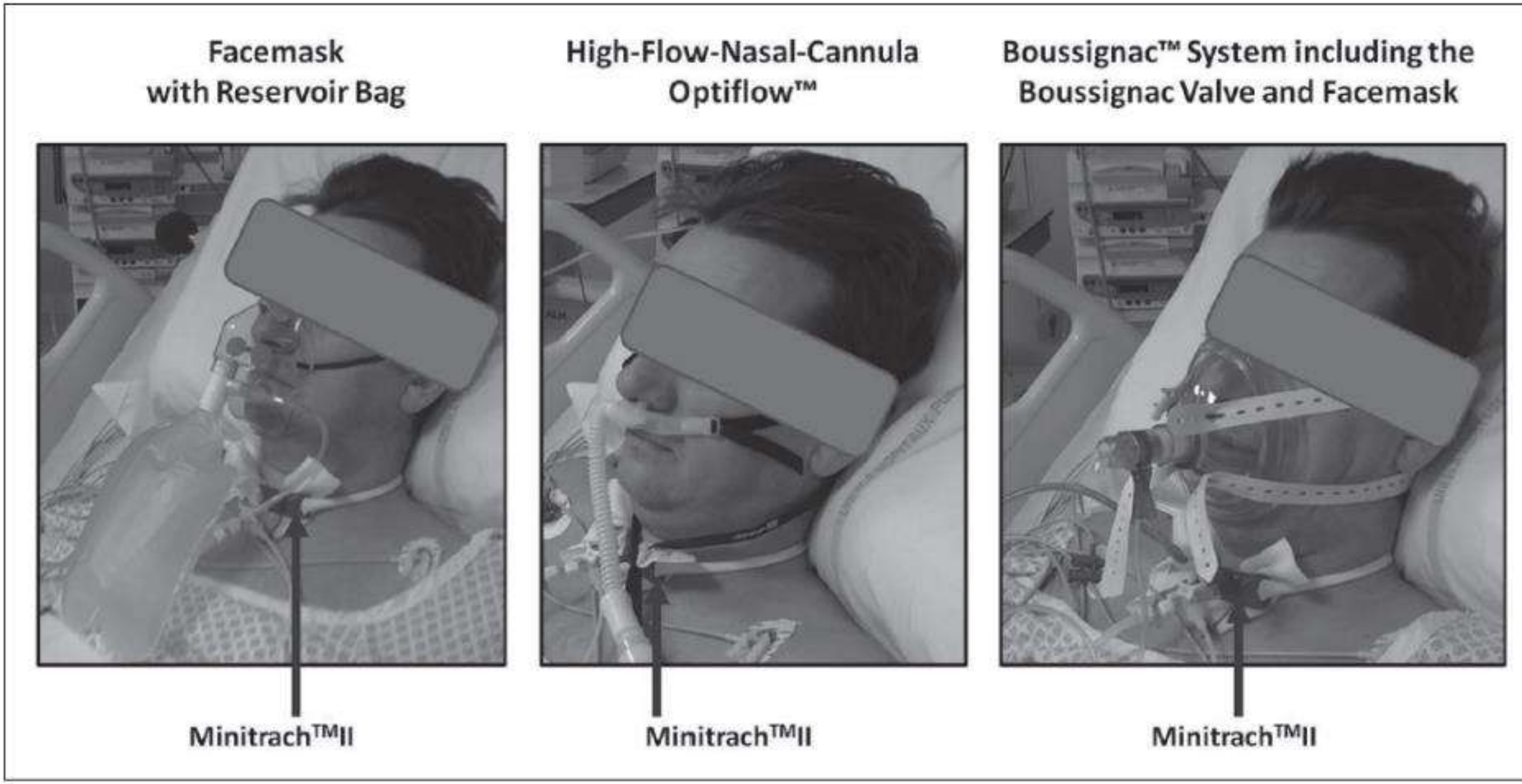
- Pts scheduled for elective cardiac surgery
- Positive linear relationship between flow and pressure
- Airway pressure was significantly greater in the mouth-closed position than the mouth-open position

  ($p < 0.001$)



Parke et al. Respir Care 2011;56(8):1151–1155

Comparison of three high flow oxygen therapy delivery devices: a clinical physiological cross-over study



Chanques G. Minerva Anestesiol. 2013;79(12):1344-55

Methods

- Cross-over in 10 ICU pts using 3 oxygen flow-rates (15, 30 and 45 L/min) and two airway-tightness conditions (open and closed mouth)
- Airway-pressures and FiO2 were measured by a tracheal-catheter inserted through the hole of a tracheotomy tube
- Comfort was evaluated by self-reporting.

Chanques G. Minerva Anestesiol. 2013;79(12):1344-55

Chanques G. Minerva Anestesiol. 2013;79(12):1344-55

Chanques G. Minerva Anestesiol. 2013;79(12):1344-55

Results

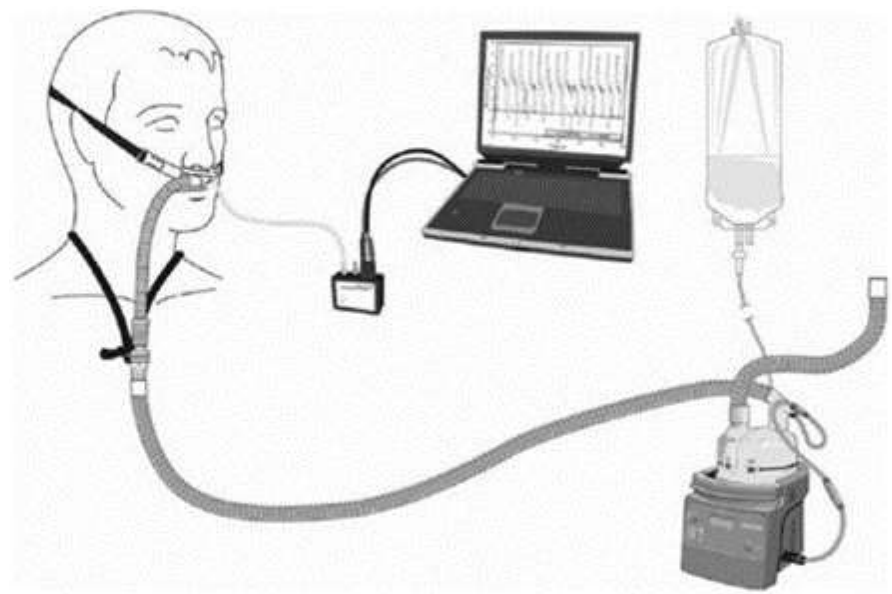
- Boussignac provided the highest mean tracheal pressure (13.9 cmH20) compared to Optiflow (2 cmH2O, P<0.001)
- Boussignac provided both positive inspiratory and expiratory airway-pressures, whereas Optiflow provided only positive expiratory airway-pressure
- FiO2 - highest value was obtained for both Optiflow and facemask (90%) compared to Boussignac (80%), P<0.01
- On mouth-opening, mean airway-pressure decreased with Optiflow only (2 vs. 0.6 cmH2O, P<0.001). Opening the mouth had little impact on FiO2
- Discomfort-intensities were low for both Optiflow and reservoir-bag-facemask compared to Boussignac, P<0.01

Chanques G. Minerva Anestesiol. 2013;79(12):1344-55

Pressures Delivered By Nasal High Flow Oxygen During All Phases of the Respiratory Cycle

Rachael L Parke RN MHSc and Shay P McGuinness MB ChB

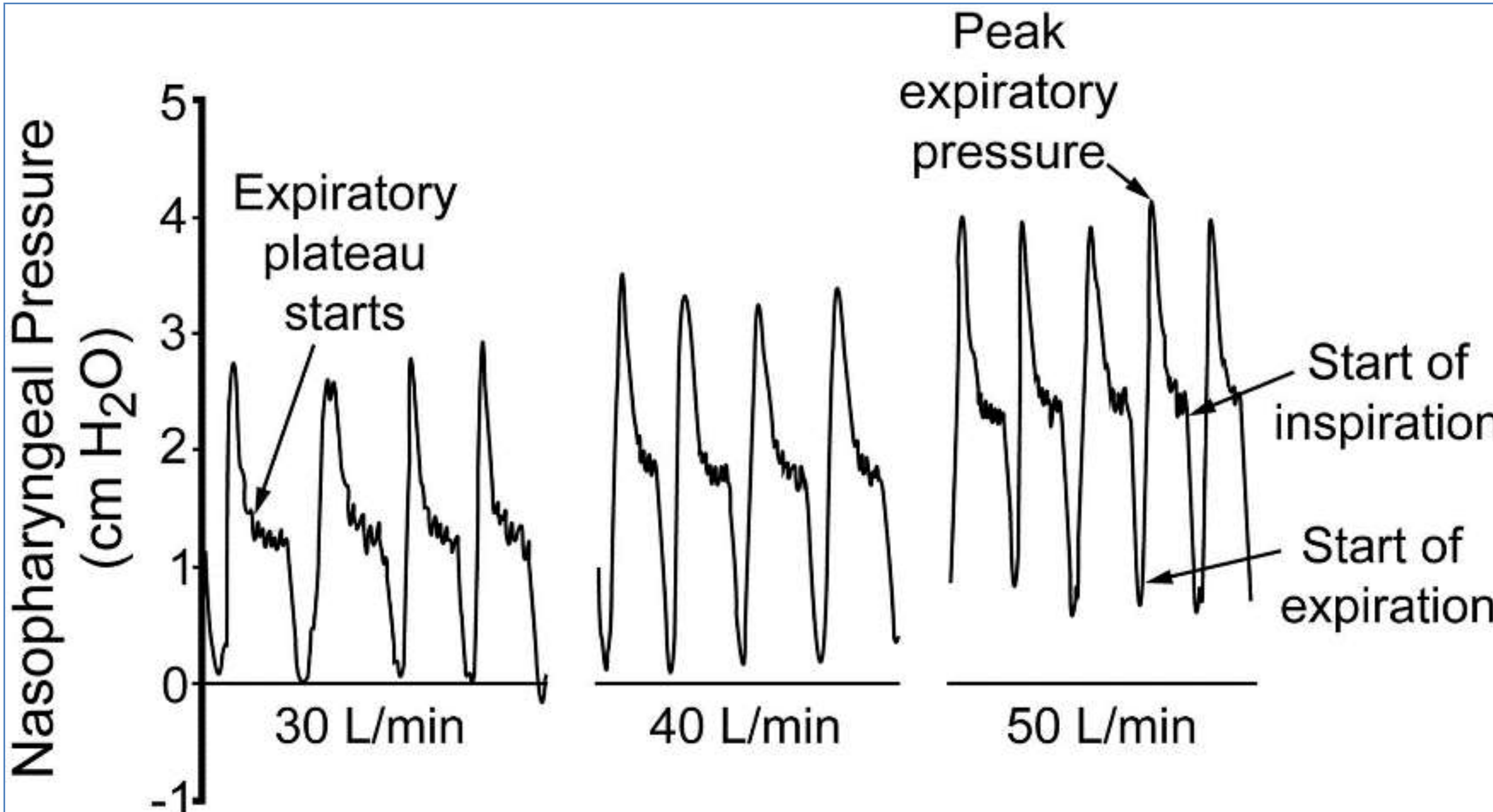
- 15 pts scheduled for elective cardiac surgery
- Nasopharyngeal pressure measurements using gas flows of 30, 40, and 50 L/min
- Mouth closed



Respir Care 2013;58(10):1621–1624

Table 2. Airway Pressures Delivered With Nasal High Flow Oxygen

Flow L/min	Airway Pressure (cm H_2O)	Average Plateau Pressure (cm H_2O)	Peak Expiratory Pressure (cm H_2O)	Average Expiratory Pressure (cm H_2O)	Average Inspiratory Pressure (cm H_2O)
30	1.52 ± 0.6	1.71 ± 0.73	3.01 ± 1.18	2.1 ± 0.83	0.55 ± 0.38
40	2.21 ± 0.8	2.48 ± 0.94	3.81 ± 1.45	2.88 ± 1.04	1.11 ± 0.51
50	3.10 ± 1.2	3.41 ± 1.24	4.86 ± 1.79	3.81 ± 1.33	1.77 ± 0.69



High-Flow Oxygen, PEEP, and the Berlin Definition of ARDS: Are They Mutually Exclusive?

- High-flow oxygen generates PEEP, often at levels greater than 5 cm H20
- Many patients on this therapy could theoretically meet the Berlin definition for ARDS
- Studies assessing NIV in ARDS should include patients on HFNC

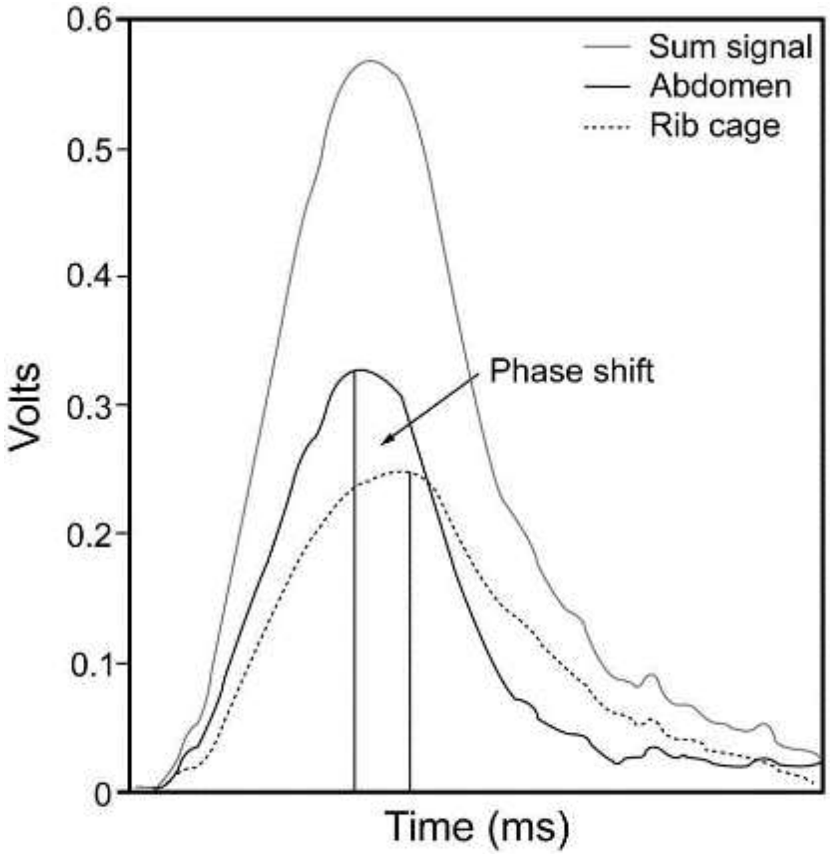
Chertoff J. Am J Respir Crit Care Med. 2017. doi: 10.1164/rccm.201701-0005LE

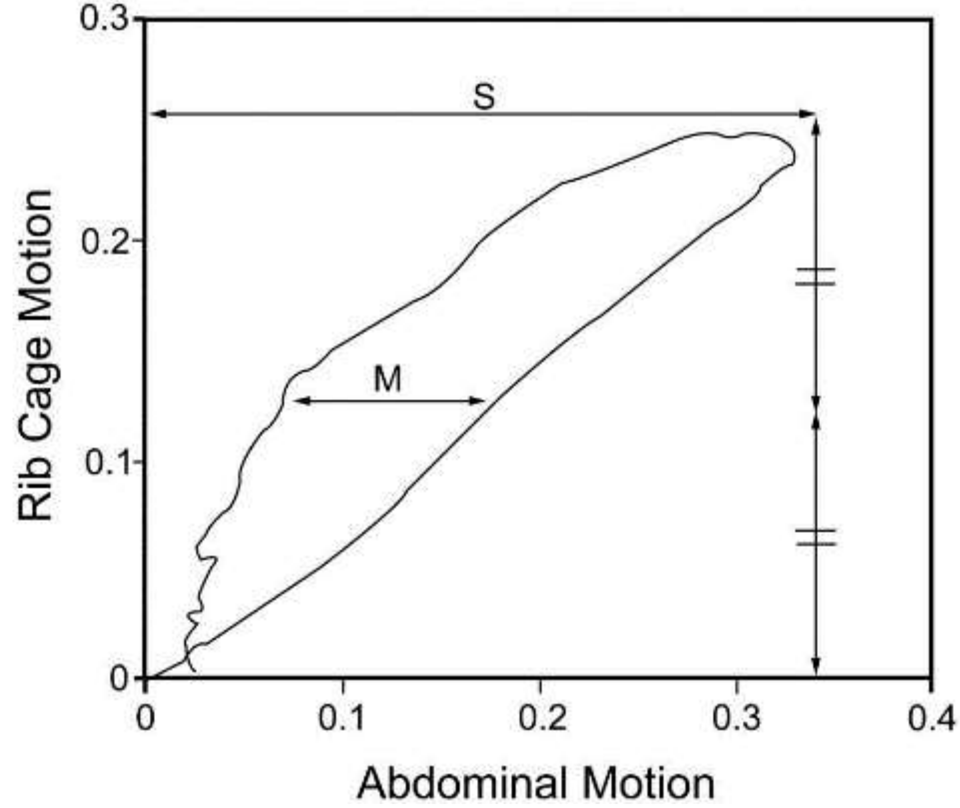
Effect of High-Flow Nasal Cannula on Thoraco-Abdominal Synchrony in Adult Critically Ill Patients

Taiga Itagaki MD, Nao Okuda MD, Yumiko Tsunano MD, Hisakazu Kohata MD, Emiko Nakataki MD PhD, Mutsuo Onodera MD, Hideaki Imanaka MD PhD, and Masaji Nishimura MD PhD

- 40 adult subjects requiring oxygen therapy in the ICU
- Low-flow O2 (up to 8 L/min) was administered via oronasal mask for 30 min, followed by HFNC at 30–50 L/min
- Respiratory inductive plethysmography transducer bands were circumferentially placed: one around the rib cage, and one around the abdomen
  - Movement of the rib-cage and abdomen
  - Sum signal represented tidal volume (VT)
  - Ratio of maximum compartmental amplitude (MCA) to VT
  - Phase angle

Respir Care 2014;59(1):70 –74





Konno-Mead diagram of abdominal motion versus ribcage motion. Phase angle (θ) =$\sin^{-1}$(M/S) Asynchrony produces a wide open loop. Synchronous ribcage/ abdominal motion has a phase angle of 0°, and paradoxical motion has a phase angle of 180°.

Respir Care 2014;59(1):70 –74

Results

Ventilation and Physiologic Variables During Oronasal Mask Oxygen Therapy Versus High-Flow Nasal Cannula

	Oronasal Mask	High-Flow Nasal Cannula	*P*
Flow, L/min	5 (5–5)	40 (35–40)	< .001
F_{IO_2}	0.39 (0.40–0.40)	0.36 (0.34–0.40)	.02
Breathing frequency, breaths/min	25 (22–27)	21 (18–24)	< .001
pH	7.46 (7.41–7.50)	7.46 (7.41–7.50)	.06
P_{aO_2}, mm Hg	97 (78–130)	101 (77–116)	.75
P_{aCO_2}, mm Hg	36 (33–40)	36 (34–40)	.22
Mean blood pressure, mm Hg	88 (77–101)	87 (73–97)	.21
Heart rate, beats/min	89 (78–104)	91 (79–102)	.32
Mouth closure: poor/fair/good, no.	NA	17/12/11	NA
MCA/V_T	1.02 (1.01–1.05)	1.00 (1.00–1.02)	< .001
Phase angle, °	19.3 (11.0–26.8)	12.6 (6.4–25.9)	.047

•HFNC improved thoraco-abdominal synchrony, by improving the phase angle and the ratio of maximum compartmental amplitude to tidal volume.
•HFNC also significantly reduced breathing frequency in patients with moderate hypoxemic respiratory failure

Respir Care 2014;59(1):70 –74

Preliminary trials

Effect of Low Flow and High Flow Oxygen Delivery on Exercise Tolerance and Sensation of Dyspnea*

A Study Comparing the Transtracheal Catheter and Nasal Prongs

Naresh A. Dewan, M.D., F.C.C.P.; and C. William Bell, Ph.D.

- 10 subjects who were already receiving TTO
- Each subject underwent 4 TMTs in a single-blind randomized fashion on 2 separate days
- Use of high-flow O2 via both transtracheal catheter and NP significantly increased exercise tolerance in COPD patients when compared to low-flow oxygen

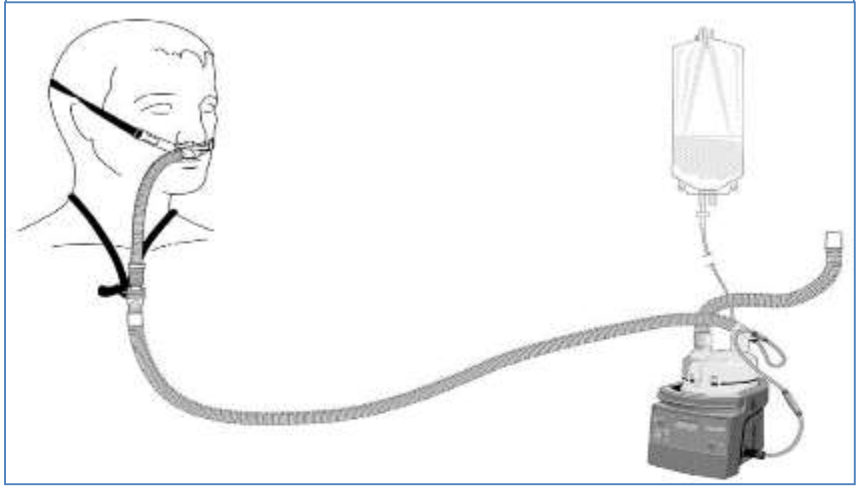
Chest. 1994;105(4):1061-5.

A Preliminary Randomized Controlled Trial to Assess Effectiveness of Nasal High-Flow Oxygen in Intensive Care Patients

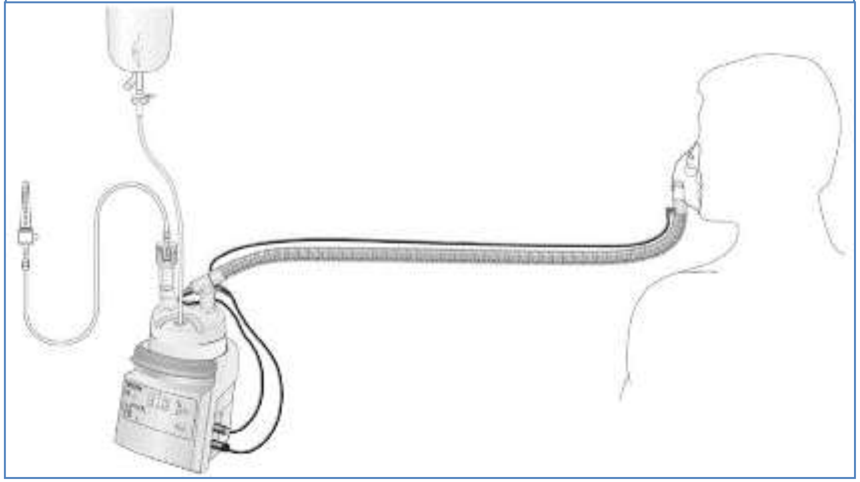
- AIM
  - To compare the effectiveness of HFNC to humidified high-flow face mask (HFFM) oxygen therapy
- Methods
  - prospective randomized comparative study in a 24-bed cardiothoracic and vascular ICU
  - 60 pts with mild to moderate hypoxemic RF were enrolled

Parke et al. Respir Care 2011;56(3):265–270.

HFNC



HFFM



	Patients (n)	Mean Desaturations (no.)	Mean Desaturations Per Patient	Mean Hours on Treatment	Mean Desaturations Per Hour
HFFM	14	26	1.86	55.3	0.47
HFNC	19	15	0.79	73.1	0.21

Parke et al. Respir Care 2011;56(3):265–270.

- RESULTS
  - More HFNC pts succeeded on their allocated therapy compared with HFFM patients (p = 0.006)
  - Significantly fewer desaturations (p = 0.009) in the HFNC group
  - 5 out of the 12 patients who failed on HFFM therapy were switched to HFNC as a “rescue therapy”. 4 of these patients were able to avoid NIV by using HFNC

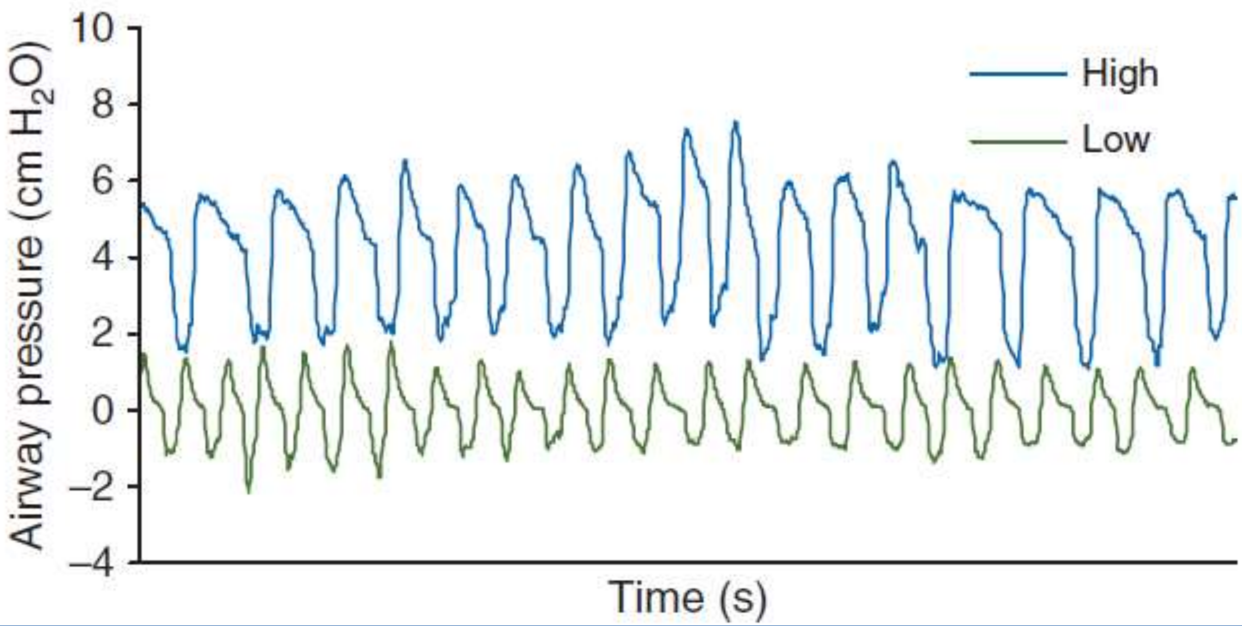
> this study NHF was more successful than HFFM in the treatment of mild to moderate hypoxemic respiratory failure. We hypothesize that the difference in NIV rate found in this study is attributable to positive pressure delivered by the Optiflow system. The results and lessons learned

Parke et al. Respir Care 2011;56(3):265–270.

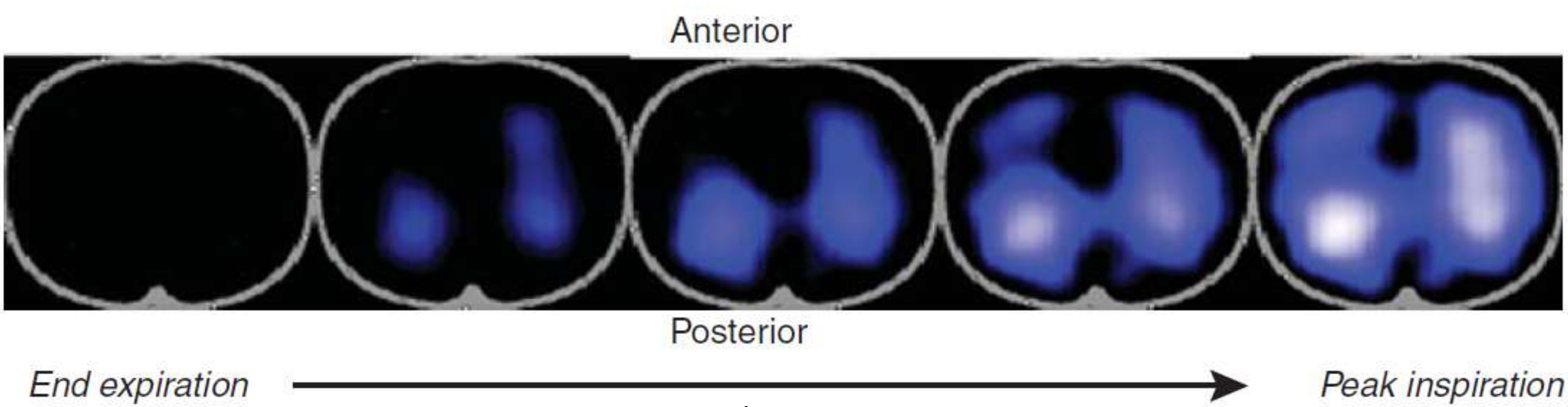
Oxygen delivery through HFNC increase EELV and reduce respiratory rate in post-cardiac surgical patients

- AIM
  - To assess the effects of HFNC compared with low-flow O2 therapy on airway pressure (Paw) and end-expiratory lung volume (EELV)
- Methods
  - 20 pts prescribed HFNC post-cardiac surgery
  - Electrical impedance tomography (EIT) was used to assess changes in lung volumes and EELV
  - Impedance measures, Paw, Pao2/FIo2 ratio, RR and modified Borg scores were recorded first on low-flow oxygen and then on HFNC

Corley et al. Br J Anaesth. 2011;107(6):998-1004



Oropharyngeal airway pressure tracing on HFNC and low-flow oxygen over 1 min. For this pt, mean airway pressure on HFNC was 4.4 cm H2O and on low-flow oxygen was 0 cm H2O.



EIT ventilation images

Results

Variable	Low-flow oxygen [mean (SD)]	HFNC [mean (SD)]	Mean difference [mean (SD)]	95% confidence interval	*P*-value
End-expiratory lung impedance (units)	419 (212.5)	1936 (212.9)	1517 (46.6)	1425, 1608	<0.001
Mean airway pressure (cm H_2O)	−0.3 (0.9)	2.7 (1.2)	3.0 (1.3)	2.4, 3.7	<0.001
Respiratory rate (bpm)	20.9 (4.4)	17.5 (4.6)	−3.4 (2.8)	−2.0, −4.7	<0.001
Borg score					
0–10	2.7 (2.6)	1.9 (2.3)	−0.8 (1.2)	−0.1, −1.4	0.023
Tidal variation (units)	1512 (195.0)	1671 (195.1)	159 (21.6)	117, 201	<0.001
Pa_{O_2}/FI_{O_2} ratio (mm Hg)	160 (53.7)	190.6 (57.9)	30.6 (25.9)	17.9, 43.3	<0.001

- A strong correlation was determined between Paw and EELV
- An increase in EELI by 25.6%, suggesting an increase in EELV and FRC
- Tidal variation increased suggesting an increase in tidal volume
- Mean reduction in respiratory rate
- Improved PaO2/FiO2 ratio
- Patients with a higher BMI showed a greater increase in mean EELI (and therefore EELV)

Corley et al. Br J Anaesth. 2011;107(6):998-1004

Beneficial effects of humidified high flow nasal oxygen in critical care patients: a prospective pilot study

- AIM
  - To evaluate the efficacy and outcome of HFNC compared to conventional HFFM in patients with acute respiratory failure
- Methods
  - Pilot prospective monocentric study
  - 38 pts exhibiting ARF
  - Requiring more than 9 l/min of oxygen output to achieve a SpO_2 >92%
    - those achieving < 92% were also included in the absence of criteria for immediate intubation
  - Persistent signs of respiratory distress
    - RR > 25 bpm, thoraco-abdominal asynchrony and supraclavicular retraction despite oxygen administration
- Baseline demographic and clinical data, as well as respiratory variables at baseline and various times after HFNC initiation during 48 h, were recorded

Sztrymf et al. Intensive Care Med; 2011 (37):1780–1786

RESULTS

- HFNC was associated with significant improvements in RR, HR, measures of WoB and improved oxygenation ($p \leq 0.05$)
- PaO2 was significantly higher 1 hr after commencing HFFNC
- PaO2/FiO2 ratio was improved at both the 1-hr and 24-hr time points
- Success rate of HFNC (to avoid escalation as reported by attending physician) was over 66%
- Intolerance was never a cause HFNC cessation

Sztrymf et al. Intensive Care Med; 2011 (37):1780–1786

Benefits of HFNC

- Improved patient comfort and tolerance
  - Roca et al. 2010
- Greater therapy success than with face masks
  - Parke et al. 2011
- Improved lung volumes
  - Corley et al. 2011
- Reduced respiratory rates
  - Corley et al. 2011, Roca et al. 2010, Sztrymf et al. 2011
- Improved oxygenation with fewer desaturations
  - Parke et al. 2011, Corley et al. 2011, Roca et al. 2010

Clinical Uses

- Acute Respiratory Failure
- Immunocompromised patients
- DNI/DNR
- Pre-intubation
- Post-extubation
- Emerging uses

Acute Respiratory Failure

Study	Design	Population	N	Main Results
Roca 2010	Cohort study, HFNC 20–30 L/min vs FM	Hypoxemic ARF	20	Improved comfort; improved oxygenation
Sztrymf 2011	Cohort, unselected patients. HFNC 50 L/min vs FM	Hypoxemic ARF	38	Improved oxygenation Decreased RR
Sztrymf 2012	Cohort, unselected patients. HFNC 20-30 L/min vs FM	Hypoxemic ARF	20	Improved oxygenation, Decrease in HR, dyspnea, respiratory distress, and thoracoabdominal asynchrony
Parke 2013	HFNC vs FM	Hypoxemic ARF	60	Decreased treatment failure (defined as need for NIV) from 30 to 10 %. Fewer desaturation episodes
Rello 2012	Cohort study (post hoc)	Hypoxemic ARF (2009 A/H1N1v outbreak)	20	9/20 (45 %) success (no intubation). All 8 patients on vasopressors required intubation within 24 h. After 6 h of HFNC, non-responders had lower PaO2/FiO2 values
Messika 2015	Observational, single-center study	ARDS	45	40 % intubation rate. HFNC failure associated with higher SAPS II, development of additional organ failure, and trends toward lower PaO2/FiO2 values and higher RR
Frat 2015 **FLORALI**	Multicenter, open-label RCT with 3 groups: HFNC, usual oxygen therapy (face mask), or NIV	Hypoxemic ARF, PaO2/FiO2 ≤300	310	Intubation rate was 38 % with HFNC, 47 % with standard oxygen, and 50 % with NIV. **Decreased 90-day mortality with HFNC**
Nagata 2015	Retrospective before/after study of HFNC	Hypoxemic ARF	172	Reduced need for intubation (100 vs 63 %, $p < 0.01$)
Kang 2015	Patients intubated after HFNC	Hypoxemic ARF	175	In patients intubated early, lower mortality (39.2 vs 66.7 %), higher extubation success (37.7 vs 15.6 %), and more ventilator-free days. Early intubation was associated with decreased ICU mortality

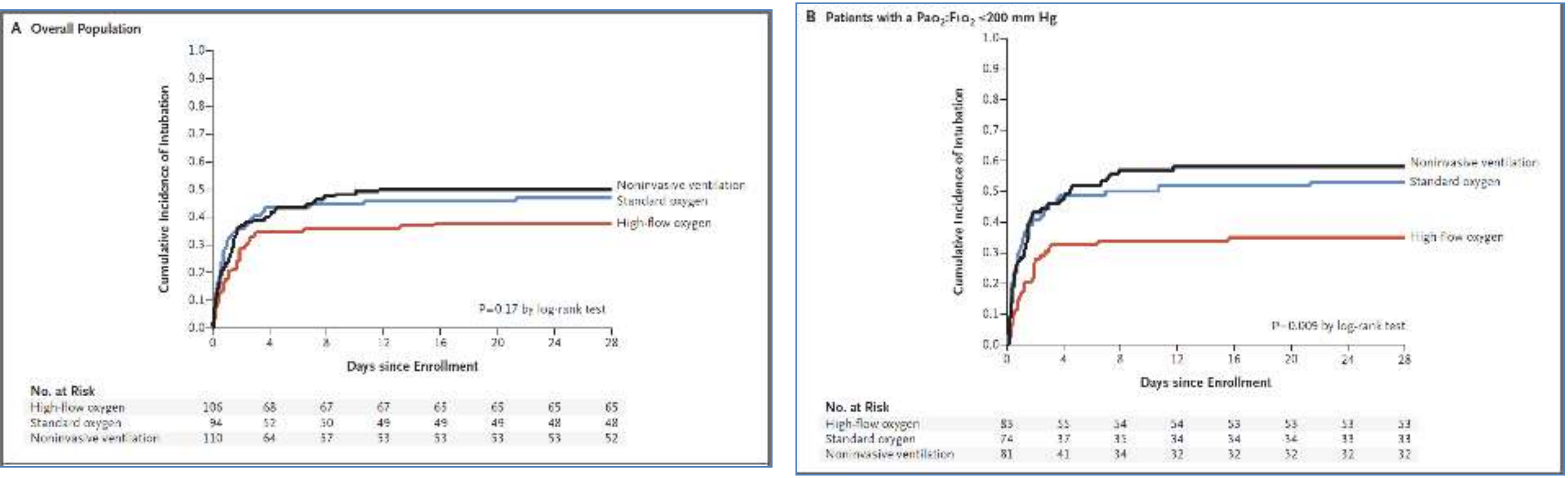
The NEW ENGLAND JOURNAL of MEDICINE
ESTABLISHED IN 1812 JUNE 4, 2015 VOL. 372 NO. 23

High-Flow Oxygen through Nasal Cannula in Acute Hypoxemic Respiratory Failure

- Florali Study - multicenter, open-label RCT; 23 ICUs in France and Belgium
- N = 310
- Acute hypoxemic RF
  - RR >25 & P/F ≤ 300, while the patient was breathing O2 @ ≥ 10 10L/min for at least 15 min, Paco2 ≤ 45 mm Hg, and an absence of clinical history of underlying chronic respiratory failure
- 3 arms – HFNC, NRM, NIV
- Primary outcome - proportion of patients intubated at D28
- Secondary outcomes - all-cause mortality in the ICU and at 90 days and the number of ventilator-free days at day 28

N Engl J Med. 2015;372(23):2185-96

Results



1. Intubation rate – HFNC - 38%; NRM - 47%; NIV – 50% (P = 0.18 for all comparisons)

2. No. of ventilator-free days at D 28 was significantly higher in the HFNC group (24±8 days, vs. 22±10 in the standard- oxygen group and 19±12 in the NIV group; P = 0.02)

3. The hazard ratio for death at 90 days was 2.01 with standard oxygen versus high-flow oxygen (P = 0.046) and 2.50 (95% CI, 1.31 to 4.78) with NIV versus high-flow oxygen (P = 0.006).

4. Comfort levels more with HFNC

N Engl J Med. 2015;372(23):2185-96

Failure of High-flow Nasal Cannula therapy may delay intubation and increase mortality

- Different numbers of patients with each etiologic category
- COPD pts were included
- Technical management issues
- Some patients were being managed in wards
- ICU mortality increased and not 28 day mortality
- Median duration of HFNC in the >48-h group was 126 h in comparison with 10 h in the<48-h group
  - -(Median duration of HFNC before intubation in different series ranged from 4 to 17.5 h)

Kang et al. Intensive Care Med; 2015(41):623–632

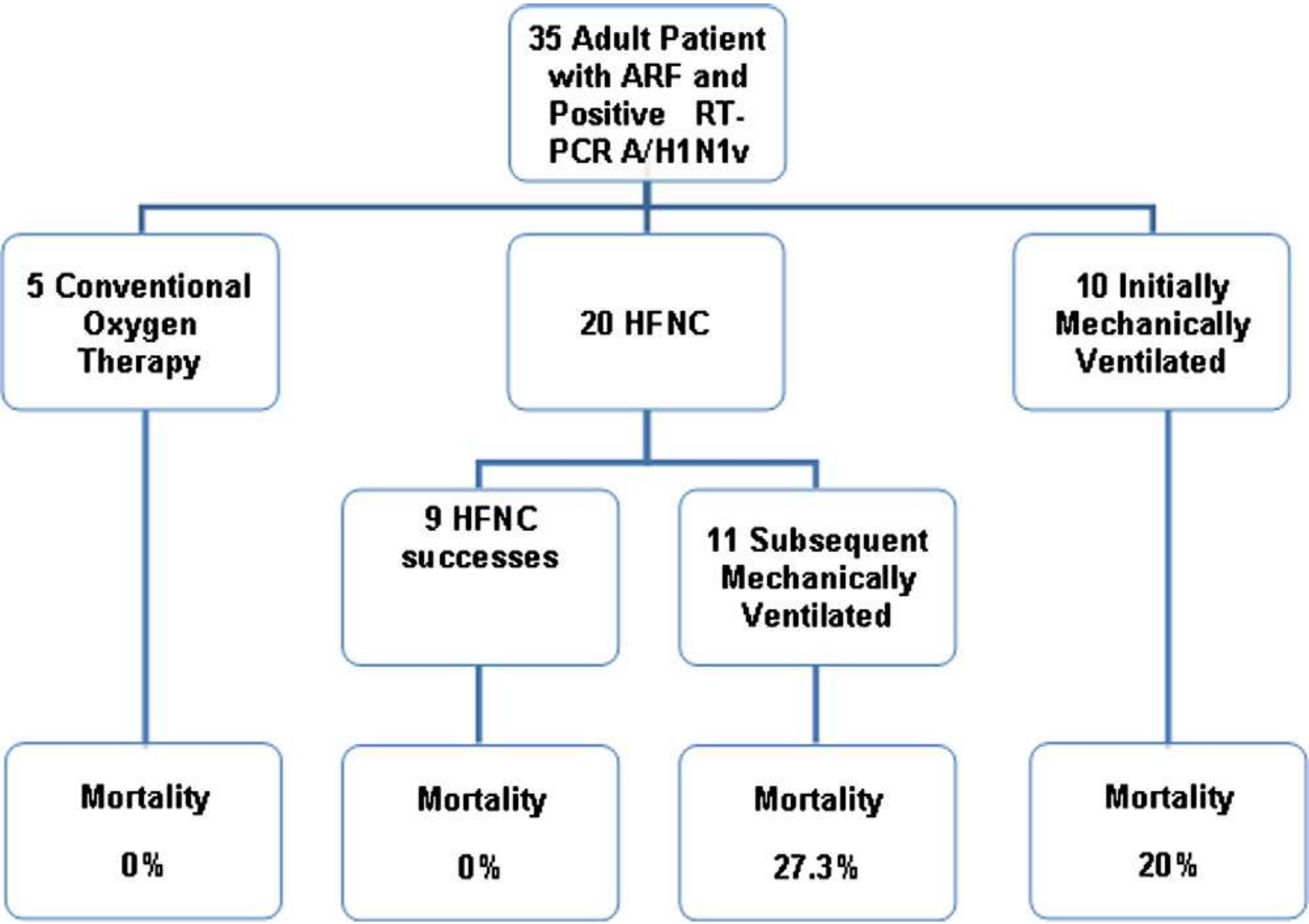
Lessons learnt

- Close monitoring of patients under HFNC is mandatory
- Early identification of failure
- Do not use for un-validated indications
  - (ac on chronic resp failure)
- Clinical signs (within the first 60 min of HFNC initiation) for HFNC failure
  - RR
  - use of accessory respiratory muscles
  - thoraco-abdominal asynchrony

High-flow nasal therapy in adults with severe acute respiratory infection. A cohort study in patients with 2009 influenza A/H1N1v

- Single-center post hoc analysis (CRIPS)
- HFNC was indicated in the presence of acute RF
  - unable to maintain spO2 > 92% with > 9 L/min FM
- Nonresponders were defined by their need of subsequent MV
- 20/25 patiens qualified for HFNC
- Successful in 9 (45%)

Rello et al. Journal of Critical Care; 2012 (27): 434–439



Rello et al. Journal of Critical Care; 2012 (27): 434–439

Table 2 Respiratory parameters 6 hours after initiation of HFNC in 20 patients with SARI

	Patients with HFNC success (n = 9)	Patients with HFNC failure (n = 11)
RR (breaths/min)	21 (20-25)	21 (12-31)
PaO_2/FIO_2 (mm Hg) *	135 (84-210) *	73 (56-81) *
SpO_2 (%)	98 (97-98)	94 (91-99)
$PaCO_2$ (mm Hg)	38 (36-38)	37 (28-43)
Total delivered flow (L/min) (**)	25 (20-30)	30 (30-35)

* $P < .05$ for the comparison between patients with successful HFNC vs failure

** $P = .12$ for the comparison between patients with successful HFNC vs failure

Rello et al. Journal of Critical Care; 2012 (27): 434–439

Lessons learnt

- Patients with an RR more than 30 may be an early indicator for the early use of HFNC
- All 8 patients on vasopressors required intubation within 24 hours
- After 6 hrs of HFNC, nonresponders presented a
  - lower P/F ratio (median, 135 [interquartile range, 84-210] vs 73 [56-81] mm Hg $P < 0.05$)
  - Higher flow rate
- No secondary infections were reported in health care workers
- No nosocomial pneumonia occurred during HFNC O2 therapy
- Odd point – all 5 pts with chronic resp conditions (Asthma/COPD) showed success though none had hypercapneic failure

Table 1. Demographics, Clinical Features, and Outcomes of Subjects With ARDS Treated via HFNC

	All Subjects With ARDS (N = 45)	HFNC Success (n = 27)	HFNC Failure (n = 18)	P
Age, median (IQR), y	57.9 (38.7–74.2)	46.1 (39–75.2)	62.8 (37.1–72.6)	.89
Males, n (%)	22 (49)	13 (48)	9 (50)	.86
At least one comorbid condition, n (%)	27 (60)	14 (52)	14 (78)	.08
Chronic heart failure	5 (11)	2 (7)	3 (17)	.33
COPD	5 (11)	3 (11)	2 (11)	> .99
Neurodegenerative disease	4 (9)	3 (11)	1 (6)	.52
Reason for HFNC oxygen therapy, n (%)				
Pneumonia	36 (80)	23 (85)	13 (72)	.44
ALI of extra-pulmonary origin	4 (9)	2 (7)	2 (11)	.67
Toxic ARDS	5 (11)	2 (7)	3 (17)	.33
At least one associated organ failure, n (%)	20 (44)	7 (26)	13 (76)	.002
Hemodynamic	11 (24)	2 (7)	9 (50)	.001
Kidney	12 (27)	6 (22)	6 (33)	.59
Neurological	4 (9)	0	4 (22)	.01
SAPS II score, median (IQR)	36 (24–44)	29 (22–37)	46 (29–61.5)	.001
Highest breathing frequency, median (IQR), breaths/min	34 (30–40)	33 (30–40)	37 (29–40)	.57
Initial P_{aO_2}/F_{IO_2}, median (IQR)	137 (88.5–208.5)	145.3 (97.5–223.5)	115.3 (84–177.1)	.26
Lowest P_{aO_2}/F_{IO_2}, median (IQR)	108.6 (73–137.1)	124 (93–217)	91.5 (64–129.5)	.02
HFNC oxygen therapy duration of < 24 h, n (%)	22 (49)	10 (37)	12 (67)	.05
Duration of therapy, median (IQR), h	24 (12.5–50)	32 (16–53)	20 (12–31)	.16
ICU stay, median (IQR), d	4 (3–12.5)	3 (2–5)	13.5 (5.5–19)	.001
Alive at ICU discharge, n (%)	35 (78)	26 (96)	9 (50)	.001
Alive at day 28, n (%)	33 (71)	24* (89)	9 (50)	.003

Messika et al. Respir Care 2015;60(2):162–169

Extent of pleural effusion on chest radiograph is associated with failure of high-flow nasal cannula oxygen therapy

Yasutaka Koga [a,*], Kotaro Kaneda [a], Ichiko Mizuguchi [a], Takashi Nakahara [a], Takashi Miyauchi [a], Motoki Fujita [b],

- Single-center retrospective study
- 29 of 73 experienced HFNC failure
- Pleural effusion and SOFA scores were independently associated with HFNC failure in multivariate analysis
  - Pleural Effusion (OR, 1.49; P = .01)
  - SOFA (OR, 1.33; P =.02)

J Crit Care. 2016; (32):165-9

ROX Index

- 2-center prospective observational cohort study performed over a 4-yr period
- 157 pts with severe pneumonia
- ROX (Respiratory rate-OXygenation) - ratio of SpO_2/FIO_2 to RR
- 12 hrs after HFNC onset, ROX index demonstrated the best prediction accuracy
  - area under the ROC curve 0.74; $P<.002$
  - ROX index ≥ 4.88 is a determinant of HFNC success in patients with pneumonia (HR, 0.273; $P=.002$)

Roca et al. J Crit Care. 2016 Oct;35:200-5

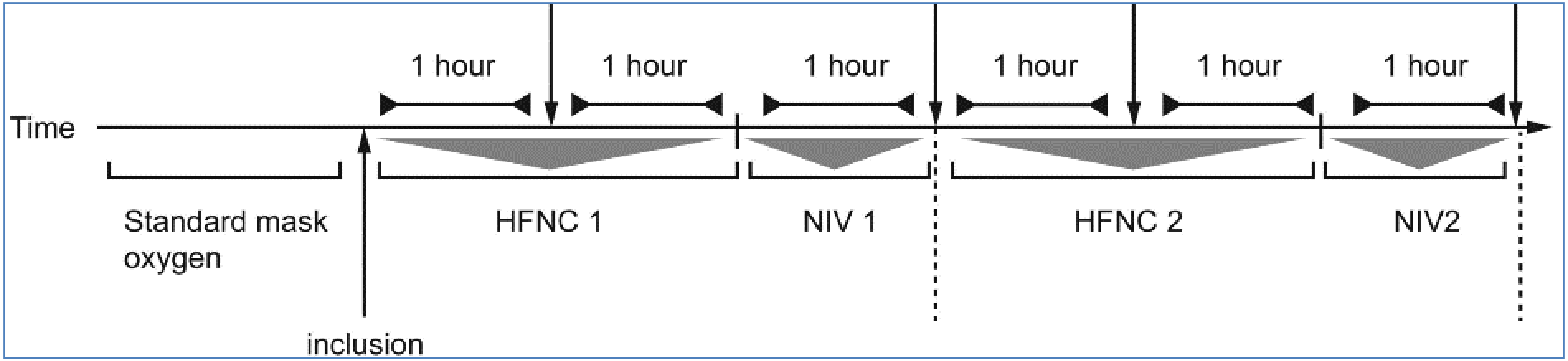
Studies in ED

Study	Design	Population	N	Main Results
Lenglet 2013	Patients with ARF (>9 L/min oxygen or clinical signs of respiratory distress) Prospective, observational study	Hypoxemic ARF	17	Decreased dyspnea and RR and improved oxygenation
Rittayamai 2015	RCT of HFNC vs standard oxygen for 1 h	Hypoxemic ARF	40	Decreased dyspnea and improved comfort

Sequential Application of Oxygen Therapy Via High-Flow Nasal Cannula and Noninvasive Ventilation in Acute Respiratory Failure: An Observational Pilot Study

Jean-Pierre Frat MD, Benjamin Brugiere MD, Stéphanie Ragot PharmD PhD,

- Prospective observational study
- 28 subjects with AHRF, including 23 with ARDS



- HFNC may be used as a bridge between NIV sessions, with the aim of pursuing a coupled noninvasive strategy of ventilation without a marked impairment of oxygenation

Respir Care 2015;60(2):170 –178

Efficacy of High-flow Nasal Cannula Therapy in Intensive Care Units: a meta-analysis of physiological and clinical outcomes

- Meta-analysis to compare the physiological and clinical outcomes of HFNC with standard O2 or conventional NIV in ICUs

- 18 articles with 2004 patients

Liesching et al. J Intensive Care Med. 2017:885066616689043

Results - HFNC with standard O2

<table>
<tr><th>No difference</th><th>Modestly improved</th><th>Significantly improved</th></tr>
<tr><td>O2 sat
(95.0% vs 93.8%, P = .27)</td><td rowspan="3">Respiratory Rate
(21.6 vs 24.7, P = .06)</td><td rowspan="2">Heart Rate
(89.1 vs 98.4, P = .03)</td></tr>
<tr><td>PaO2/FIO2
(217.7 vs 161.9, P = .29)</td></tr>
<tr><td>PaCO2
(38.3 vs 39.3, P = .33)</td><td rowspan="2">PaO2
(104.5 vs 90.0 mm Hg, P = .04)</td></tr>
<tr><td>pH (7.416 vs 7.419, P .90)</td><td rowspan="3">ICU mortality
(OR = 0.69, P = .13)</td></tr>
<tr><td>Discomfort
(1.19 vs 1.44, P .44)</td><td rowspan="2">Dyspnea
(2.7 vs 4.3, P = .05)</td></tr>
<tr><td>ICU stay
(4.0 vs 4.5 days, P = .90)</td></tr>
</table>

Liesching et al. J Intensive Care Med. 2017:885066616689043

Results - HFNC with NIV

- PaO_2 (106.9 vs 134.2 mm Hg, $P = .02$)
- PaO_2/FIO_2 (178.4 vs 220.0 mm Hg, $P = .02$)
- $PaCO_2$ (37.7 vs 39.2 mm Hg, $P = .04$)
- ICU mortality (odds ratio = 0.39, 95% CI: 0.19-0.82, $P = .01$)
- Slightly lower intubation rate and ICU mortality

- Patients with pneumonia may benefit from HFNC in reduced RR, HR, dyspnea, discomfort, intubation rate, ICU mortality, ICU stay, and improved PaO_2

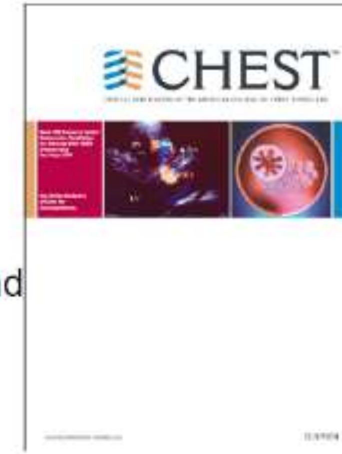
Liesching et al. J Intensive Care Med. 2017:885066616689043

The effect of HFNC oxygen therapy on mortality and intubation rate in acute respiratory failure: a systematic review and meta-analysis

- 14 trials were eligible for inclusion in the review
- 9 trials were used in the meta-analysis, including a total of 2,507 subjects
- No difference in mortality or intubation rates
- HFNC associated with improved patient comfort and dyspnea scores
- Required information size was not reached
- Including conventional oxygen and NIV in the same comparative with HFNC may not have been appropriate

Monro-Somerville et al. Crit Care Med. 2017 Apr;45(4):e449-e456

Accepted Manuscript



Can high-flow nasal cannula reduce the rate of endotracheal intubation in adult patients with acute respiratory failure compared with conventional oxygen therapy and noninvasive positive pressure ventilation? A systematic review and meta-analysis

Yue-Nan Ni, Jian Luo, He Yu, Dan Liu, Ni Zhong, Jiangli Cheng, Bin-Miao Liang, Zong-An Liang

- Controlled studies that compared HFNC with NIV and COT in adult patients having ARF
- 18 trials with a total of 3881 patients

Chest. 2017. pii: S0012-3692(17)30011-9.

Results

	HFNC vs COT	HFNC vs NIV
Rate of endotracheal intubation	OR 0.47, 95% CI 0.27~0.84, P=0.01	OR 0.73, 95% CI 0.47~1.13, P=0.16
ICU mortality	OR 0.65, 95% CI 0.37~1.13, P=0.13	OR 0.63, 95% CI 0.34~1.18, P=0.15
ICU LOS	MD 0.30, 95% CI -0.78~1.37, P=0.59	MD -0.01, 95% CI -0.97~0.96, P=0.99
Subgroup analysis of HFNC in patients after extubation (n=2,741) Rate of re-intubation	OR 0.39, 95% CI 0.23~0.65, P=0.0003	OR 1.07, 95% CI 0.82~1.40, P=0.60

Chest. 2017. pii: S0012-3692(17)30011-9.

Clinical practice points

- Data insufficient, conflicting and equivocal
- HFNC can be used as a first line therapy in Acute hypoxemic respiratory failure
  - Exclude hypercapneic patients
- Use early in ARF (RR>30/min)
- Close monitoring – early identigication of failure
  - 1st hour – RR, use of acc ms, asynchrony
  - 6hrs – P/F ratio, higher flow/FiO2 requirement
  - 12h – ROX Index
- Markers of failure – shock, neurological dysfunction, lower P/F, SAPS/SOFA, Pl effusion
- Pts who fail HFNC will usually do it in 1st 24h

Use of HFNC in Immunocompromised patients

- Mortality in immunocompromised patients with hypoxemic ARF is significantly higher
- Respiratory management that aims to avoid intubation/invasive MV is of major interest
- Studies so far have discrepant results
- Feasibility and safety of HFNCO in immunocompromised
  - Lee et al. (2015) – Hematological malignancies
  - Epstein et al. (2011) – Solid tumours

- Equipoise between HFNCO, NIV, and COT
- Future trials warranted to demonstrate survival benefits

HFNC vs BiPAP for Persistent Dyspnea in Patients With Advanced Cancer

- To examine the changes in dyspnea, physiologic parameters and adverse effects with these modalities
- HFNC or BiPAP for two hours
- 30 pts enrolled (1:1) and 23 (77%) completed the assigned intervention
- Both modalities improved parameters studied but no difference between them
  - Oxygen saturation was only improved by HFNC

Hui et al. J Pain Symptom Manage. 2013 Oct;46(4):463-73.

HFNC vs Venturimask in immunocompromised patients with hypoxemic ARF

- Multicenter, parallel-group randomized controlled trial in 4 ICUs
- Inclusion criteria
  - Hypoxemic ARF (hypercapneic patients excluded)
  - Immunosuppression - solid or hematological malignancy, steroid or other immunosuppressant drug therapy or HIV infection
- Randomized to 2 h of HFNC or Venturi mask
- Primary endpoint - need for IMV or NIV during the 2-h period
- Secondary endpoints -comfort, dyspnea, and thirst

Lemiale et al. Critical Care; 2015 (19):380

Results

- 100 patients, including 84 with malignancies
- no significant difference in any outcome

	HFNO group (n = 52)	Venturi mask group (n = 48)	*P* value
Primary endpoint			
Number (%) of patients requiring mechanical ventilation	8 (15 %)	4 (8 %)	0.36
Noninvasive mechanical ventilation	6[a]	3[a]	
Invasive mechanical ventilation	4	2	
Secondary endpoints, median [25th–75th percentile]			
Discomfort VAS score[b] at 120 min	3 [1–5]	3 [0–5]	0.88
Dyspnea VAS score[b] at 120 min	3 [2 – 6]	3 [1–6]	0.87
Thirst VAS score[b] at 120 min	6 [3–8]	6 [5 – 9]	0.40
Respiratory rate at 120 min, breaths/min	25 [22–29]	25 [21–31]	
Heart rate at 120 min, beats/min	98 [90–110]	99 [83–112]	0.43

Lemiale et al. Critical Care; 2015 (19):380

Effect of Noninvasive Ventilation vs Oxygen Therapy on Mortality Among Immunocompromised Patients With Acute Respiratory Failure

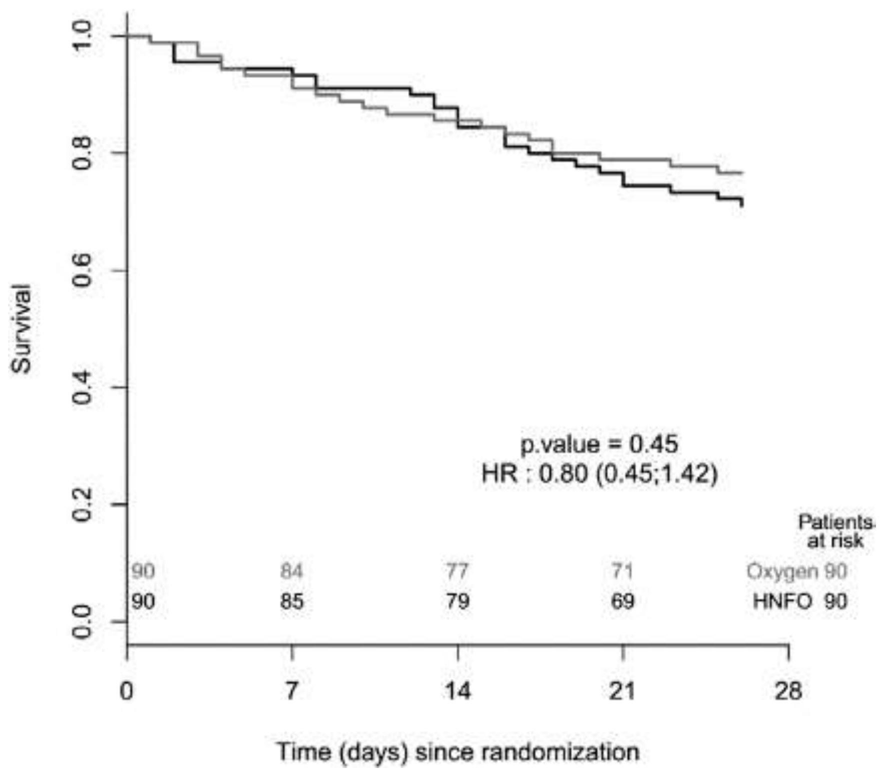
A Randomized Clinical Trial

- 374 pts, 191 NIV, 183 oxygen therapy group
- HFNC was given to 141 patients overall (37.7%) and was used more often in the oxygen group (44.3%) than NIV group (31.4%) (*P = .01)*
- 15 of 60 (25.4%) died in the NIV group, vs 26 of 81 (32.1%) in the oxygen group (*P = .36)*

Lemiale et al. iVNIctus Trial. JAMA. 2015;314(16):1711-1719

Post-hoc analysis

- No difference in intubation rates / survival between HFNC and O2 group.



Lemiale et al. Crit Care Med 2017; 45:e274–e280

Effect of non-invasive oxygenation strategies in immunocompromised patients with severe acute respiratory failure: a post-hoc analysis of a randomised trial

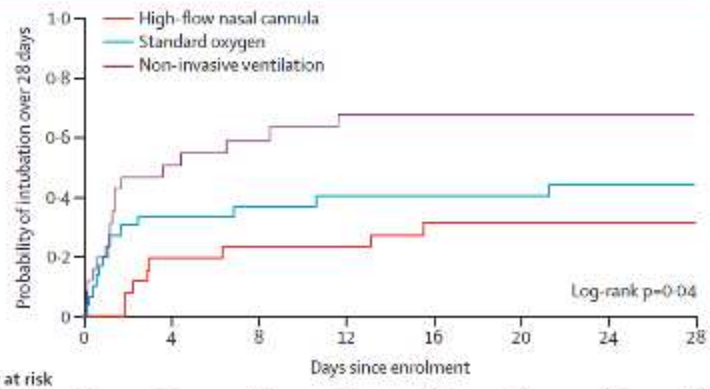
Jean-Pierre Frat, Stéphanie Ragot, Christophe Girault, Sébastien Perbet, Gwénael Prat, Thierry Boulain, Alexandre Demoule, Jean-Damien Ricard, Rémi Coudroy, René Robert, Alain Mercat, Laurent Brochard, Arnaud W Thille, for the REVA network

- Compare outcomes of immunocompromised patients with ARF treated with standard oxygen with those treated with HFNC alone or HFNC + NIV

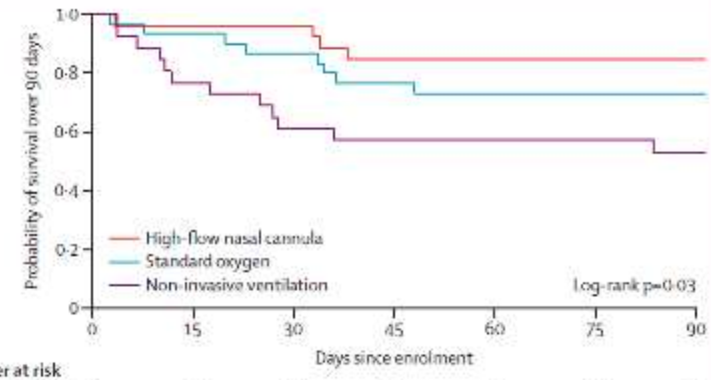
- 82 immunocompromised patients
  - 30 standard oxygen, 26 HFNC, and 26 NIV + HFNC

Lancet Respir Med. 2016 Aug;4(8):646-52

Results



Number at risk	0	4	8	12	16	20	24	28
High-flow nasal cannula group	26	21	20	20	18	18	18	18
Standard oxygen group	30	20	18	17	17	17	16	16
Non-invasive ventilation group	26	12	10	8	8	8	8	8



Number at risk	0	15	30	45	60	75	90
High-flow nasal cannula group	26	25	25	22	22	22	22
Standard oxygen group	30	28	26	23	22	22	22
Non-invasive ventilation group	26	20	16	15	14	14	13

- Intubation at 28 days
  - HFNC -8/26 (31%); Std O2 -13/30 (43%); NIV+HFNC- 17/26 (65%) (p=0·04)
- After multivariable logistic regression, the 2 factors independently associated with intubation and mortality were age and use of NIV as first-line therapy

Lancet Respir Med. 2016 Aug;4(8):646-52

DNI

- Retrospective analysis of 50 pts
- DNR/DNI, clinical evidence of respiratory distress, hypoxemia, and mild or compensated hypercapnia ($PaCO2 \leq 65$ and $pH \geq 7.28$)

	BEFORE HFNC	HFNC
PaO_2 (mm Hg)	66.5 (39-121)	95.4
$PaCO_2$ (mm Hg)	42.3 (26-65)	40.2
pH	7.42 (7.30-7.51)	7.43
Respiratory rate (breaths/min)	30.6	24.7[a]
Oxygen saturation (%)	89.1	94.7[a]
Escalation to NIV [patients(%)]		9/50 (18%)

P< 0.01

Peters et al. Respir Care 2013;58(4):597–600

HFNC use preceding ETI

- Almost 30 % of ETI are associated with serious adverse events
- The most frequently reported complication (26 %) is severe desaturation under 80 %, notably for hypoxemic patients
- Preoxygenation before ETI is a crucial stage
- Existing methods – NRM, NIV
  - No large RCTs
  - Interrupted during laryngoscopy
  - Aerophagy
  - Pt co-operation with NIV
- HFNC has theoretical advantages
- Observational studies have demonstrated feasibility and equivalence between 3 strategies

Jaber S et al. Crit Care Med. 2006; 34:2355–2361

Non-rebreathing bag reservoir facial mask vs HFNC before ETI

- Prospective quasi-experimental before-after study
- *N = 101;* regardless of the reasons for intubation; severe hypoxemia were excluded
- Primary outcome – the median (IQR) lowest SpO2 reached during ETI (*$p < 0.0001$*)
  - 100 % (95–100 %) in the HFNCO group
  - 94 % (83–98.5 %) *for the facial mask*
- Prevalence of desaturation events (<80 %) decreased from 14 % in the facial mask group to 2 % in the HFNC group (*$p = 0.03$*)

Miguel-Montanes et al. Crit Care Med 2015; 43:574–583

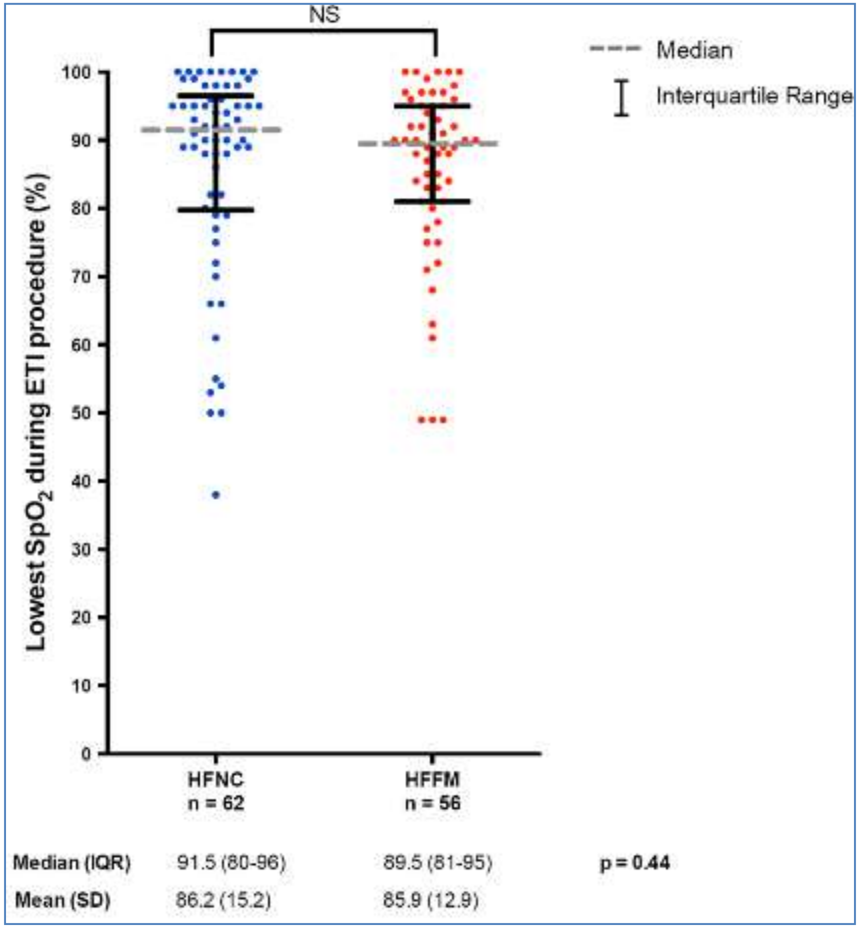
PREOXYFLOW trial

- Multicenter, randomized, open-labelled, controlled trial in 6 French ICUs; ITT
- P/F < 300 mmHg, RR ≥ 30/min, FiO2 ≥ 50 %
- 124 pts
- Primary outcome - lowest saturation throughout intubation procedure
- Secondary outcomes – adverse events related to intubation, duration of MV and death

Vourc'h et al. Intensive Care Med 2015;41(9):1538-48.

Results

- No difference in any of the outcomes
- Patient population different compared to *Miguel-Montanes study*
- Included patients with severe hypoxemia (mean PaO2/FiO2 about 120 mmHg)



FELLOW Trial

- Randomized, open-label, pragmatic trial
- 150 pts – Apnoeic oxygenation with HFNC vs usual care
- Primary outcome -lowest arterial O2 saturation b/n induction and 2 min after completion of ETI
- No difference in outcome

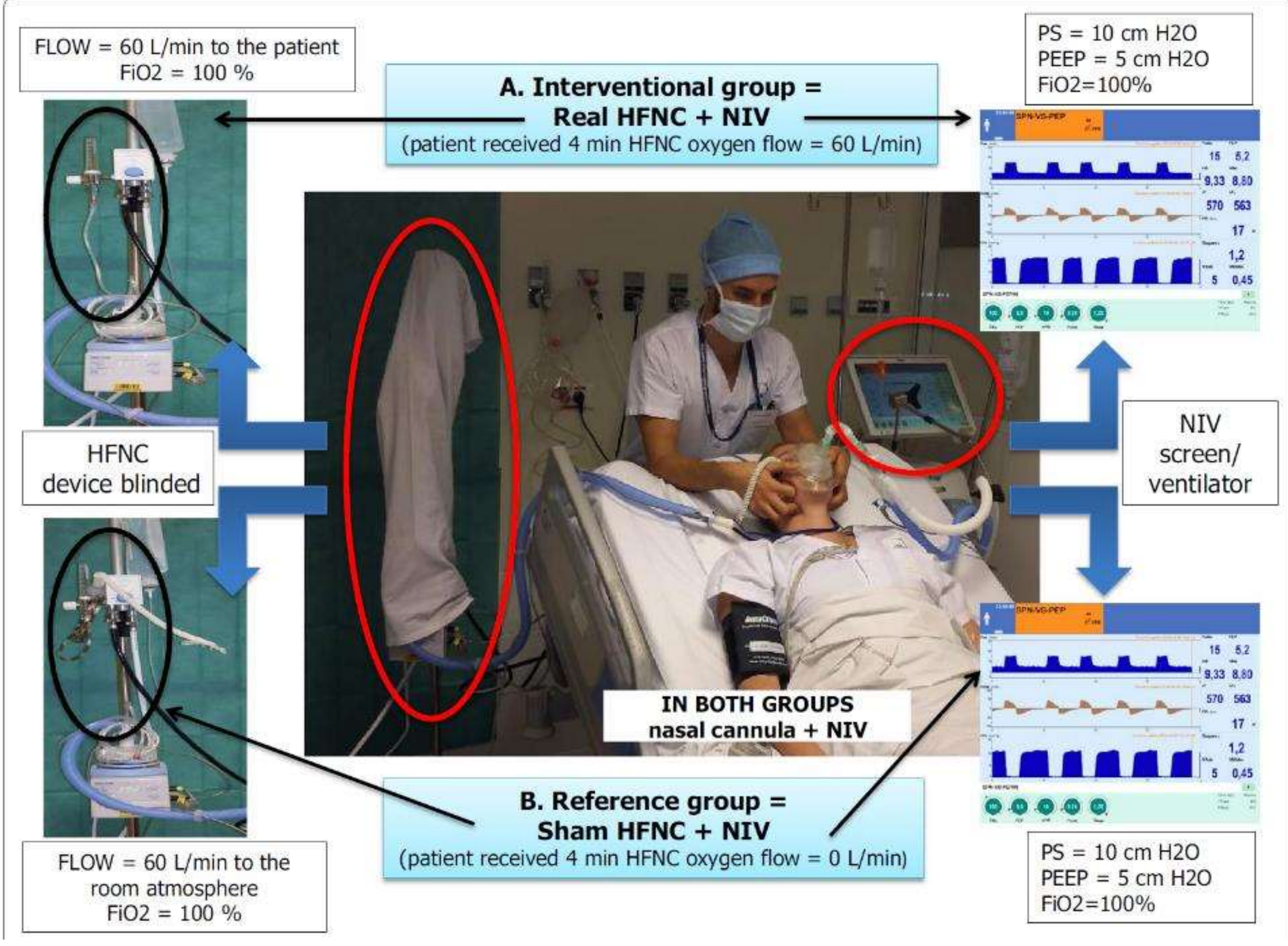
Semler et al. Am J Respir Crit Care Med. 2016;193(3):273-80.

Study	Design	Population	N	Main Results
Before intubation (for oxygenation)				
Miguel-Montanes 2015	Before (NRM)/after (HFNC) study	Adults with acute hypoxemia requiring intubation	101	Higher lowest SpO2 value during intubation (100 vs 94 %) Higher SpO2 value at the end of preoxygenation
Vourc'h M 2015	Multicenter RCT of HFNC throughout the procedure vs O2 mask	Adults with acute hypoxemia requiring intubation, PaO2/FiO2 <300, and respiratory rate ≥30/min	124	No difference in lowest SpO2 (91.5 vs 89.5 %, *p = 0.44)* No difference in intubation-related adverse events including desaturation <80 %, and mortality
Semler 2016 FELLOW	RCT of HFNC during laryngoscopy vs no O2	All adults being intubated by a fellow	150	No difference in lowest SpO2 (92 vs 90 %; *p = 0.16)* No difference in the incidence of SpO2 <90 % (45 vs 47 %; *p = 0.87)*

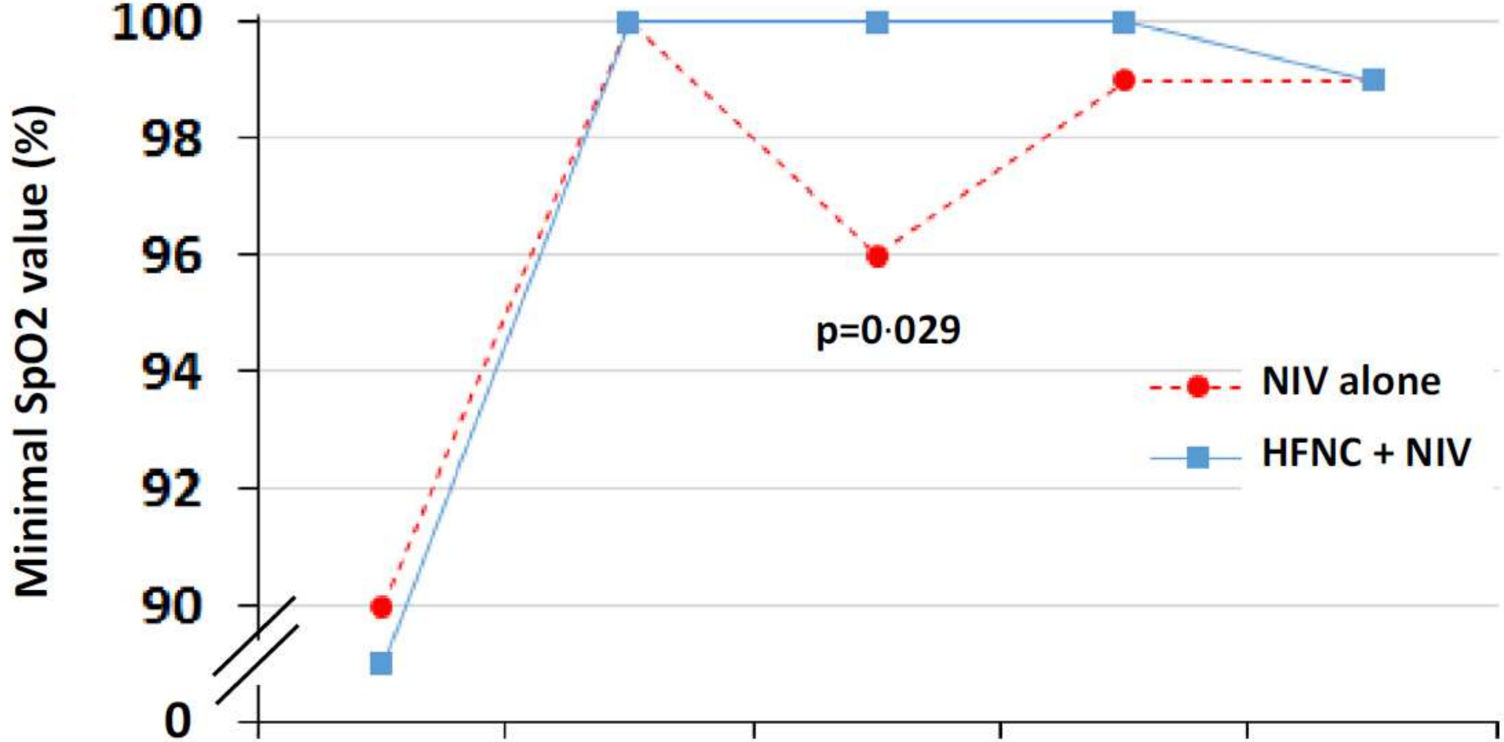
OPTINIV Trial

- Randomised, controlled, single-centre trial with assessor-blinded outcome assessment
- Intervention gp - Real HFNC + NIV – 25pts
- Comparison pp – Sham HFNC + NIV – 24 pts
- Primary outcome
  - lowest SpO2 during ETI
- Secondary outcomes
  - intubation-related complications and ICU mortality

Jaber et al. Intensive Care Med. 2016 Dec;42(12):1877-1887



FLOW = 60 L/min to the patient
FiO2 = 100 %
A. Interventional group =
Real HFNC + NIV
(patient received 4 min HFNC oxygen flow = 60 L/min)
PS = 10 cm H2O
PEEP = 5 cm H2O
FiO2=100%
HFNC
device blinded
NIV
screen/
ventilator
IN BOTH GROUPS
nasal cannula + NIV
B. Reference group =
Sham HFNC + NIV
(patient received 4 min HFNC oxygen flow = 0 L/min)
FLOW = 60 L/min to the
room atmosphere
FiO2 = 100 %
PS = 10 cm H2O
PEEP = 5 cm H2O
FiO2=100%



	Baseline	Before intubation	During intubation	Intubation + 5’	Intubation + 30’
NIV Median (IQR) Range [min-max]	90 (86-93) [73-99]	100 (96-100) [75-100]	96 (92-99) [56-100]	99 (92-100) [92-100]	99 (97-100) [93-100]
HFNC + NIV Median (IQR) Range [min-max]	89 (87-92) [78-100]	100 (99-100) [85-100]	100 (95-100) [25-100]	100 (100-100) [92-100]	99 (98-100) [89-100]
NIV Mean (SD)	89·0 (5·7)	96·2 (5·9)	91·5 (12·5)	91·3 (9·0)	97·8 (2·5)
HFNC + NIV Mean (SD)	89·6 (5·5)	98·4 (3·6)	94·6 (15·0)	92·8 (6·7)	98·1 (2·8)

Jaber et al. Intensive Care Med. 2016 Dec;42(12):1877-1887

HFNC after extubation

- To reverse postextubation atelectasis and improve oxygenation
- Observational, retrospective studies and small RCTs
  - Inconsistent results
  - Probably prevents re-intubation
  - Patient comfort and tolerance better
  - No difference in mortality

- No large RCTs or multi-centric studies

Study	Design	Population	N	Main Results
After extubation in the ICU (to avoid reintubation)				
Maggiore 2014	Double-center RCT Air entrainment mask vs. HFNC for 48 h	Patients with $PaO_2/FiO_2 \leq 300$ immediately before extubation	105	Improved oxygenation and comfort, Fewer patients had interface displacements Fewer patients required reintubation or NIV
Tiruvoipati 2010	Randomized crossover study of HFNC vs air entrainment mask	Patients ready for extubation	50	Tolerance was better with HFNCO
Rittayamai 2014	Randomized crossover study of HFNC vs non-rebreathing mask	Patients ready for extubation	17	Less dyspnea Lower respiratory and HR
Brotfain 2014	Retrospective study of HFNC vs NRM	Patients ready for extubation	67	Improved oxygenation, Fewer patients required reintubation No difference in mortality

HFNC Vs Conventional Oxygen Therapy After Endotracheal Extubation: A Randomized Crossover Physiologic Study

- N = 17 mechanically ventilated subjects
- Randomized after extubation to either
  - Protocol A (HFNC for 30 min, followed by NRM for another 30 min) -
  - Protocol B (NRM for 30 min, followed by HFNC for another 30 min)
  - Initial inspiratory flow of 35 L/min, and FiO_2 adjusted to achieve SpO_2 of at least 94% within the first 5 min
- Level of dyspnea, RR, HR, BP, SpO_2 and patient comfort were recorded

Rittayamai et al. Respir Care 2014;59(4):485–490

Parameters	HFNC (Mean ± SD)	Non-rebreathing Mask (Mean ± SD)	*P*
Subjective evaluation			
Dyspnea score	1.6 ± 1.2	2.9 ± 1.5	.04*
Comfort score	1.4 ± 0.9	1.9 ± 1.1	.07
Respiratory and gas exchange variables			
Oxygen saturation, %	98.2 ± 2.1	98.8 ± 1.8	.44
Breathing frequency, breaths/min	19.8 ± 3.2	23.1 ± 4.4	.009*
Hemodynamic variables			
Mean arterial pressure, mm Hg	95.8 ± 12.3	97.5 ± 10.2	.32
Heart rate, beats/min	89.5 ± 9.5	95.4 ± 10.4	.006*

* $P < .05$

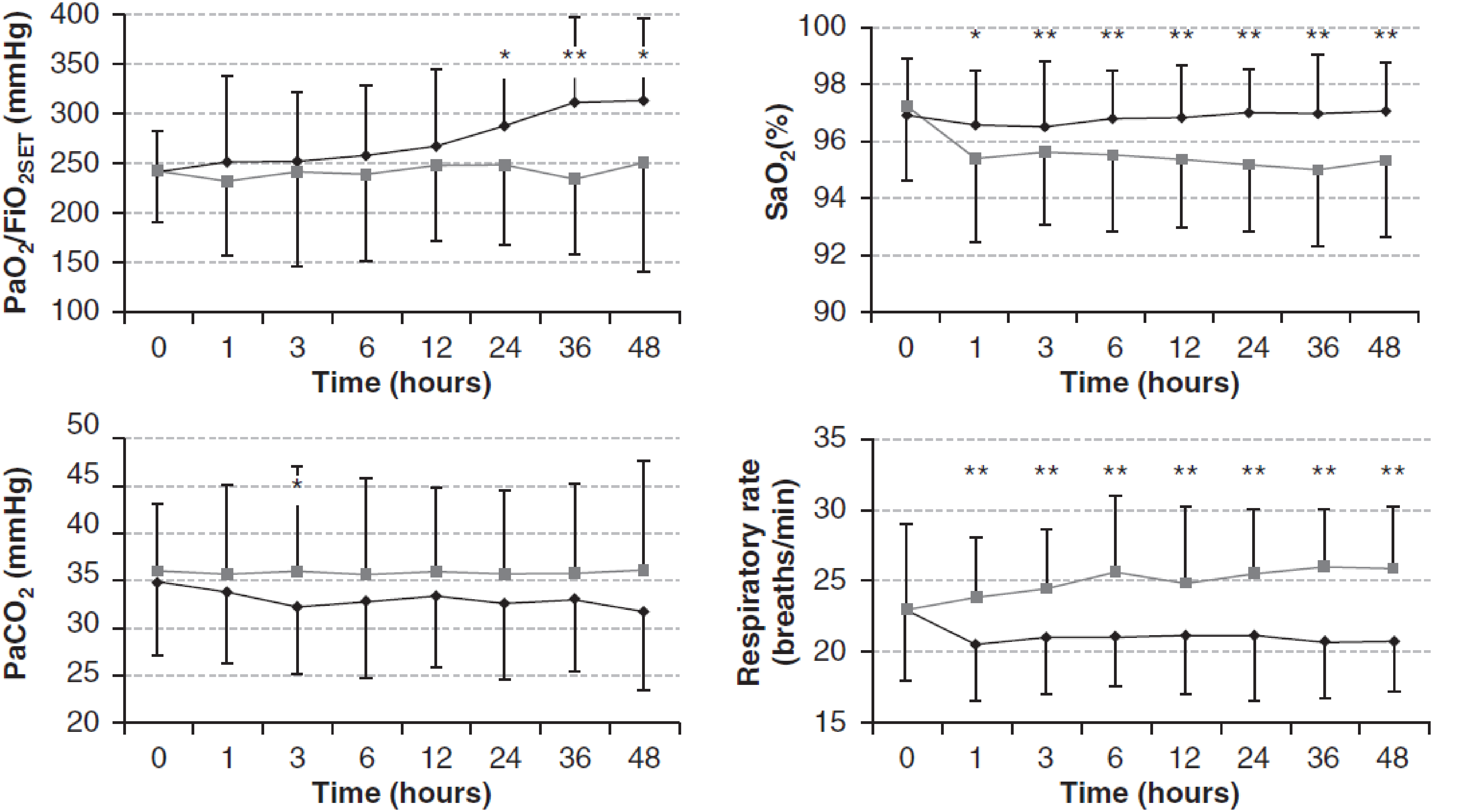
No subject was re-intubated or received NIV after completion of the study

Rittayamai et al. Respir Care 2014;59(4):485–490

Nasal High-Flow versus Venturi Mask Oxygen Therapy after Extubation Effects on Oxygenation, Comfort, and Clinical Outcome

- Randomized, controlled, open-label trial
- N=105
- P/F≤ 300 immediately before extubation
- Primary outcome – P/F after extubation
- Secondary endpoints - to assess effects on patient discomfort, adverse events, and clinical outcomes

Maggiore et al. Am J Respir Crit Care Med. 2014;190(3):282-8.



Values at t 0 were recorded at the end of the successful SBT, just before extubation
*P , 0.05; **P < 0.01.

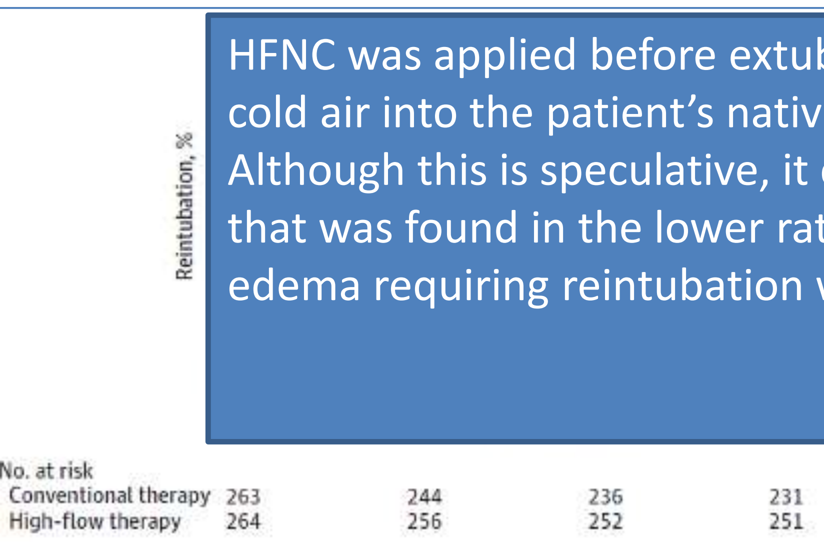
- Discomfort related both to the interface and to airways dryness was better with NHF
- Oxygen desaturations (40% vs. 75%; P , 0.001)
- Reintubation (4% vs. 21%; P = 0.01)
- Any form of ventilator support (7% vs. 35%; P , 0.001)

Maggiore et al. Am J Respir Crit Care Med. 2014

HFNC in Post-extubation management

HFNC vs COT (low-risk)

- Multicenter RCT
- N= 527
- Superiority
- Mean gas flow of 31 l/min



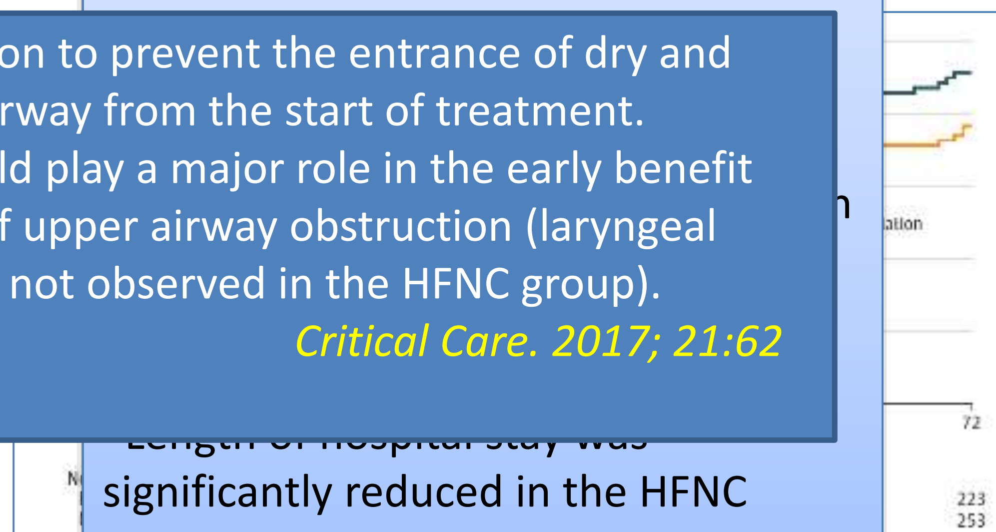
HFNC vs NIV (high-risk)

•Postextubation respiratory failure - lower rate in the HFNC group compared to the NIV group (26.9% vs 39.8%)

▪Significantly higher adverse event

HFNC was applied before extubation to prevent the entrance of dry and cold air into the patient's native airway from the start of treatment. Although this is speculative, it could play a major role in the early benefit that was found in the lower rate of upper airway obstruction (laryngeal edema requiring reintubation was not observed in the HFNC group).

Critical Care. 2017; 21:62



significantly reduced in the HFNC group

Hernández et al. JAMA. 2016;316(15):1565-1574

RINO Trial

- **Impact of Nasal High-flow vs Venturi Mask Oxygen Therapy on Weaning Outcome: a Multicenter, Randomized, Controlled Trial (RINO)**
- ClinicalTrials.gov Identifier: NCT02107183
- Salvatore Maurizio Maggiore
- Sample size - 500
- Estimated Primary Completion Date - March 2017
- Primary Outcome - Reintubation within 72 hours after extubation or at ICU discharge

Clinical Practice points

- HFNC seems to lower re-intubation rates post extubation in patients with Respiratory Failure
- It also provides better patient comfort and better oxygenation than COT
- It may be equivalent to NIV in non-hypercapneic patients with high-risk of re-intubation

Clinical studies of HFNCO in adults after postop extubation

Study	Design	Population	N	Main Results
Parke 2013	RCT of HFNC until day 2 vs FM	Heart surgery patients ready for extubation	340	Fewer patients needed escalation of respiratory support to NIV
Stephan 2015 BiPOP JAMA	Multicenter RCT of HFNC vs NIV for at least 4 h per day	Prevention or treatment of ARF after cardiothoracic surgery	830	HFNCO was not inferior to NIV No difference in ICU mortality Skin breakdown more common with NIV after 24 h
Corley 2015	RCT of HFNC vs usual care Single Centre RCT	Pts with a BMI ≥30 ready for extubation after heart surgery	155	No difference in atelectasis scores on day 1 or 5, mean PaO2/FiO2 ratio, respiratory rate, or reintubation
Futier 2016 OPERA	Multicentre RCT HFNC vs COT	Pts at moderate to high risk of postop pulmonary complications after major abd surgery	220	No difference in rates of hypoxia after 1h and during 7 day postop period
Yu 2017	RCT; HFNC vs COT	Thoracoscopic lobectomy after extubation; intermediate to high risk for PPC	110	Occurrence rate of hypoxemia with COT was twice more than that with HFNC (p<0.5)

HFNC vs COT in cardiac surgical patients: a meta-analysis

- 495 adult postextubation cardiac surgical patients
- HFNCs were associated with a significant reduction in the escalation of respiratory support (RR 0.61; P＜0.001)
- No significant differences in
  - Reintubation rate
  - Length of ICU stay

Zhu et al. J Crit Care. 2017;38:123-128

Emerging Uses

Hypercapneic Respiratory Failure

Stable chronic hypercapnic respiratory failure

- LTOT vs HFNC – PCO2 lower with HFNC with lower RR, I:E, better EELV and TV but poorer comfort levels
  - *Fraser et al. Thorax. 2016*
- LTOT vs HFNC during Sleep – HFNC produced a greater reduction in MV, reduction in CO2 levels and halved the WOB
  - *Biselli et al. J Appl Physiol. 2016*
- NIV vs HFNC – HFNC with mouth closed similar to NIV in RR, TV, breathing pattern, PCO2, comfort; inspiratory effort lower with NIV
  - *Pisani et al. Thorax 2017*
- nBiPAP/nCPAP vs HFNC – HFNC leads to flow-dependent reduction in pCO2,MV, WOB and RSBI and increase in TV
  - *Bräunlich et al. Int J Chron Obstruct Pulmon Dis. 2016*

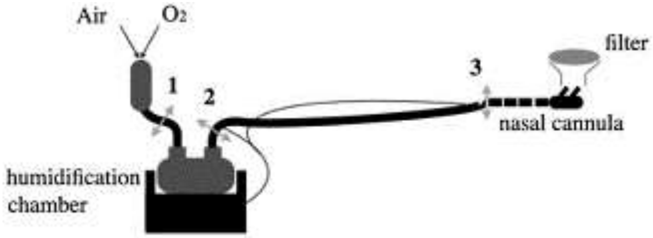
Heart Failure

- Sequential intervention prospective study
- 10 adults with NYHA class III and LVEF≤ 45%
- High flow @ 20 and 40L/min, FiO_2 21%
- IVC collapse studied (reduction>20% significant)
- Baseline - 37%; 20 lpm - 28%; 40 lpm -21% [$p<0.05$)
- Mean attributable reductions of 20% and 53%
- Changes reversible after HFNC withdrawal
- RR significantly reduced from 23 to 17 bpm (20L) and 13 bpm (40 L)
- No significant changes in other echocardiographic or clinical variables

Roca et al. J Crit Care. 2013 Oct;28(5):741-6

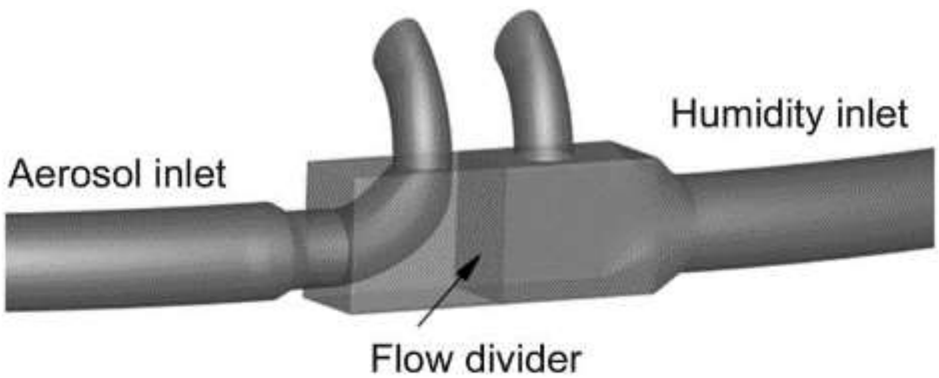
Aerosol delivery

- Drug deposition reduces with increasing flow
  - inspired doses (% of the nominal dose) were 2.5, 0.8, 0.4, and 0.2% for the adult cannula at 5, 10, 20, and 40 L/min *(Perry et al. Pediatr Crit Care Med 2013)*
- May be used for continuous aerosol bronchodilator administration in the setting of acute asthma
  - The most efficient placement of the nebulizer was upstream from the humidifier *(Re´miniac et al. J Aerosol Med Pulm Drug Deliv. 2015)*



Hess DR. Respir Care 2015;60(6):880 –893

Approaches to Improve Aerosol Delivery During HFNC



1. Enhanced condensational growth
   - Separate streams of submicron aerosol and heated humidified air to the left and right nostrils, respectively
2. Excipient enhanced growth
   - Inhaled submicron aerosol in combination with a hygroscopic excipient

Longest et al. Aerosol Med Pulm Drug Deliv 2013;26(5): 266-279
Golshahi L. Respir Care 2014;59(10):1476-1486

Bronchoscopy during HFNC use

- Technically easier compared to NIV
- Pilot RCT– stable patients (*Lucangelo et al. 2012)*
  - HFNC at 60 L/min had better PaO2, PaO2/FiO2, and SpO2 than those receiving 40 L/ min through air entrainment mask or HFNC
  - No difference b/n 40 L/min through air entrainment mask or HFNC
- Unstable pts, RCT -P/F<165 *(Simon et al. Critical Care 2014)*
  - Oxygen levels were significantly higher with NIV than with HFNC both during and after bronchoscopy
  - 19/20 patients in the HFNC gp successfully completed the procedure with no complications
- OptiBAL Study - prospective, observational multicenter trial
  - Study completed, results awaited

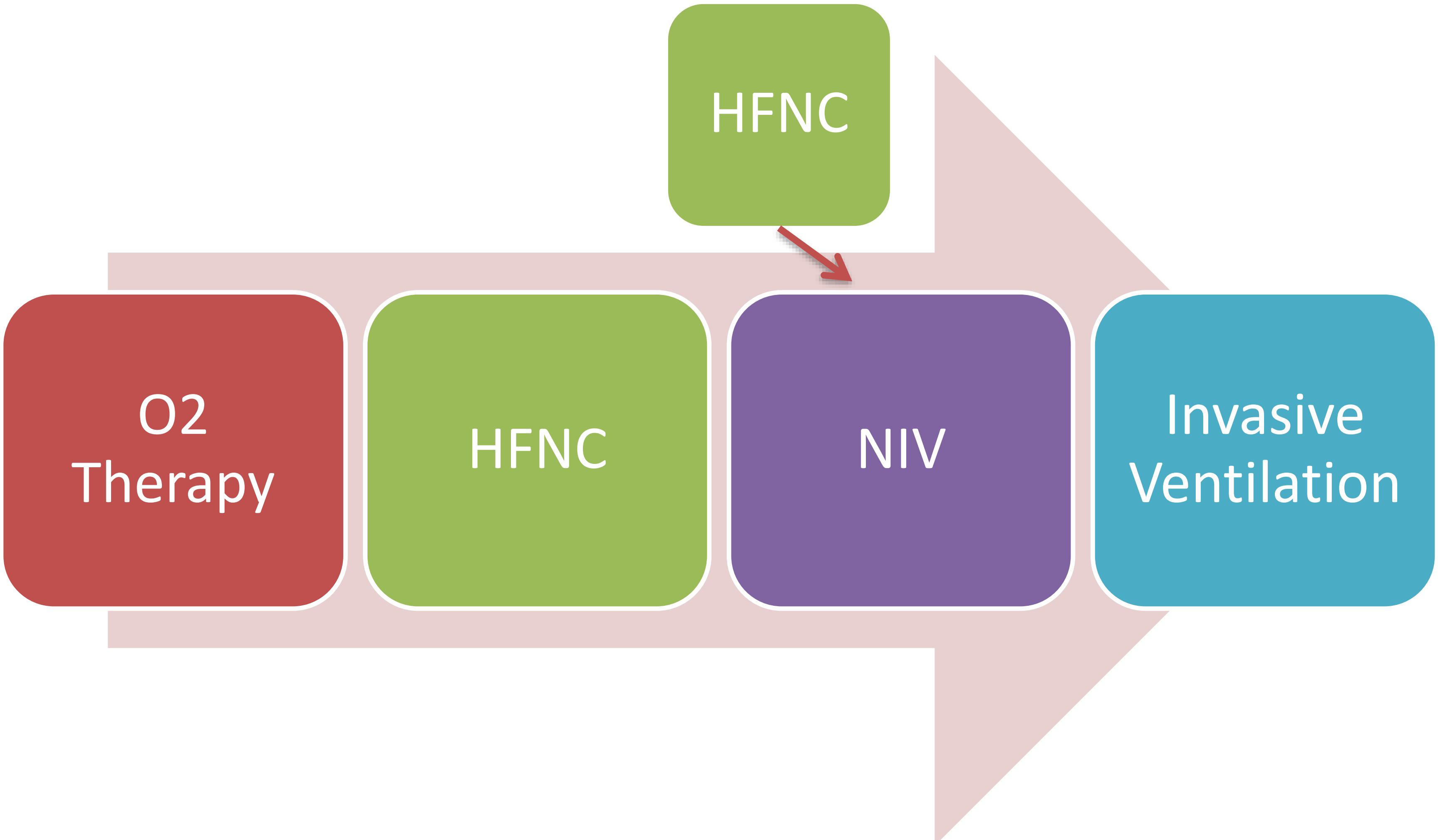
Uncertainities

- Wide variability in inclusion criteria and heterogeneity in study populations
- Primary endpoints different
  - physiological vs clinical
  - Time of endpoint measurement different
- HFNC parameters, timing and setting variable
- Variability in results
- Differences in control arm

HFNC vs NIV

NIV	HFNC
• Variable flow, fixed pressures	• Fixed flow, variable pressures
• anatomical dead space is increased	• anatomical dead space is decreased
• TV increases	• No direct effect on TV
• Comfort levels lesser	• Unequivocally more comfortable
• Feedback available, titrated objectively	• Feedback not available, titrated arbitarily

Take Home Messages



Take Home Messages

- Existing evidence cannot place HFNC as the standard of care for any clinical situation
- Acceptable modality in the continuum of Respiratory Care
- Patient selection is of utmost importance
- Timing of initiation and abandonment vital
- Excellent modality in End of Life care where mask is poorly tolerated
- Larger and better studies with clinical end-points required to formulate protocols for effective use