“Non-Invasive Positive Pressure Ventilation”
Robert M. Kacmarek PhD, RRT
Harvard Medical School
Massachusetts General Hospital
Boston, Massachusetts

Who – Indications for NPPV

Undisputed indications
- Acute Exacerbation of COPD
- Acute Cardiogenic Pulmonary Edema

General Indications for Use
- Post extubation Hypercarbic Respiratory Failure
- Hypoxemic Respiratory Failure in :
  - Immunosurpressed Patients
  - Patients Awaiting Transplantation
  - Patients Post Lung Resection
- Patients with DNI Status
- Acute Hypercapnic Respiratory Failure as a Result of Neurological or Neuromuscular Disease

Controversial Indications
- Post –Extubation Hypoxemic Respiratory Failure
- Acute Lung Injury
- Acute Respiratory Distress Syndrome
- Asthma
Brochard NEJM 1995; 333:817

- Acute exacerbation COPD
- NPPV (n = 43) vs control (n = 42)
- Five centers in Europe

<table>
<thead>
<tr>
<th></th>
<th>NPPV</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intubated</td>
<td>11 (26%)</td>
<td>31 (74%)*</td>
</tr>
<tr>
<td>Hospital Stay</td>
<td>23 ± 17</td>
<td>35 ± 33 days*</td>
</tr>
<tr>
<td>Mortality</td>
<td>4 (9%)</td>
<td>12 (29%)*</td>
</tr>
</tbody>
</table>

*p < 0.01

10/12 control and 3/4 NPPV

Deaths in intubated patients

---

NPPV Acute Exacerbation of COPD

- 15 RCT’s NPPV in COPD
- NPPV:
  - Prevents intubation
  - Decreases length of MV
  - Decreases ICU and Hosp stay
  - Decreases cost
  - Decreases mortality

Keenen JAMA 2002
NPPV Acute Exacerbation of COPD

- Standard of Care
- Should be available as first line therapy in all setting caring for COPD patients

Figure 3. Effects of Noninvasive Ventilation on Need to Intubate

Masip JAMA 2005;294:3124
MV and Heart Failure

- **CPAP - standard**
- **NPPV - ventilatory failure**
- **Intubation and invasive ventilation**
  - Active cardiac ischemia (infarction)
  - Hemodynamic instability
  - Arrhythmias
  - Depressed mental status
NPPV Acute Hypoxemic RF

- Post Operative Respiratory Failure
- Immunosuppressed Patients
- Patients Awaiting Transplantation
- Patients Post Lung Resection
- Acute Lung Injury
- Acute Respiratory Distress Syndrome

Squadrone JAMA 2005;293:589

- 209 pts developing hypoxemia (P/F < 300 mm Hg) post major abdominal elective surgery
- Randomized to CPAP vs. simple O2 therapy
- CPAP lower incidence of:
  - Intubation (1% vs. 10%, p = 0.005)
  - Pneumonia (2% vs. 10%, p = 0.02)
  - Infection (2% vs. 10%, p = 0.03)
  - Sepsis (2% vs. 9%, p = 0.03)
- No difference in ICU or Hosp LOS or mortality (0 vs. 3)
Kindgren-Milles Chest 2005;128:821

- 56 pts following elective prosthetic replacement of the thoracoabdominal aorta
- Post extubation in ICU 10 cmH\textsubscript{2}O CPAP for 12 to 24h vs. CPAP 10 min Q4h
- Fewer pulmonary complications (Pneumonia, atelectasis, \(P/F < 100\), reintubations), \(p < 0.019\)
- Hosp LOS 22±2 vs. 34±5 days, \(p < 0.048\)

HPPV-Hypoxemic Respiratory Failure

- Hilbert NEJM 2001;344:481
  - 52 Immunosuppressed patients NPPV vs. St Rx
  - Required intubation, Serious complications, Died in the ICU: better with NPPV \(p < 0.05\)
- Antonelli JAMA 2000; 283:235
  - 40 Patients awaiting transplantation NPPV vs. St Rx
  - Intubation, Length of hospitalization, Complications, ICU mortality: better with NPPV \(p < 0.05\)
- Auriant AJRCCM 2001;164:1231
  - 48 patients post lung resection
  - Intubation, Hospital mortality: better with NPPV \(p <0.05\)
Antonelli NEJM 1998; 339:429

- Hypoxemic ARF, non-immunosuppressed
  NPPV n = 32, CMV n = 32
- Survival: 50% CMV, 69% NPPV
- Complications: 66% CMV, 38% NPPV (P=0.02)
- Pneumonia/sinusitis:
  31% CMV, 3% NPPV (p=0.003)
- MV shorter NPPV (p=0.006)
- ICU stay shorter NPPV (p=0.002)

Ferrer AJRCCM 2003;168:1444

- 105 pts PO\textsubscript{2} < 60 mmHg or SpO\textsubscript{2} < 90% for > 6 hr with maximal O\textsubscript{2} 50% by venturi mask
- RCT: O\textsubscript{2} vs. NPPV, PEEP 7 ± 2, ventilating press 16 ± 3 cmH\textsubscript{2}O for 3.5 ± 2.6 days
- NPPV decreased:
  - Intubation 13(25%) vs. 28(52%) p = 0.01
  - Septic shock 6(12%) vs. 17(31%) p = 0.028
  - ICU mortality 9(18%) vs 20(39%) p = 0.028
Intubation Rate non-COPD
Keenan et al CCM 2004;32:2516

Mortality non-COPD
Keenan et al CCM 2004;32:2516
Delchaux JAMA 2000; 284:2352

- RCT acute hypoxemic RF, P/F < 300 mmHg
- N = 61 St Rx O₂ vs N = 62 CPAP
- ETI 34% CPAP vs 39% NS
- Mortality 19% CPAP vs 18% NS
- LOS 6.5 CPAP vs 6.0 NS
- Adverse events 18 CPAP vs 6, p = 0.01

Delclaux JAMA 2000; 284:2352

<table>
<thead>
<tr>
<th>Before Intubation</th>
<th>Control</th>
<th>CPAP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Facial Necrosis</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Cardiac Arrest</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td>After Intubation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nosocomial Pneumonia</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>Sinusitis</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Pneumothorax</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Stress Ulcer</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td>Total (% of patients)</td>
<td>6 (10)</td>
<td>18 (29)</td>
</tr>
</tbody>
</table>
Unsuccessful Application of NPPV in Acute Respiratory Failure

- Cardiopulmonary stress uncorrected
  - RR, $V_T$
  - HR, BP
  - accessory muscle use
- $\text{PaCO}_2$/pH/ $\text{PaO}_2$ unchanged
- If not achieved in 1 - 2 hrs of NPPV, especially in hypoxemic ARF, intubate!

Antonelli et al ICM 2001;27:1718

Predictors of failure of NPPV in acute HRF

- 8 Hospitals, Europe and USA
- 354 patients treated with NPPV, 30% intubated
- Hospital Mortality of those falling NPPV 64%
- Independent Risk Factors for Failure of NPPV:
  - SAPS II $\geq$ 35
  - > 40 years
  - ARDS
  - Pneumonia
  - P/F $\leq$ 146 mmHg after 1 hr
Mortality by Subgroup Failing NPPV

- Pulmonary ARDS 4 of 12, 33%
- Extra-pulmonary ARDS 18 of 32, 56%
- Community Acquired Pneumonia 10 of 19, 53%
- Nosocomial Pneumonia 8 of 9, 92%
- CPE 1 of 2, 50%
- Pulmonary Embolism 2 of 2, 100%
- Atelectasis 4 of 10, 40%
- Pulmonary Fibrosis 1 of 1, 100%
- Trauma 8 of 13, 64%
Schettino CCM 2008

- About 1000 patients received NPPV over the course of one year
- Three groups: Chronic use, ARF, DNI/DNR
- 144 with hypoxemic ARF (none acute heart failure or post extubation)
- 60% failed NPPV and were intubated
- Of these 64% (55) died

Schettino CCM 2008

- Acute RF 458 patients managed with NPPV
- 38% failed NPPV and required intubation
- Mortality failing 47% vs. 5.4%, p < 0.0001
- CPE 18% intubated, mortality 39%
- COPD 24% intubated, mortality 33%
- Non-COPD hypercapnia 38% intubated, mortality 0.0%
- Post extubation failure 40% intubated, mortality 32%
Primary Reason for Intubation

<table>
<thead>
<tr>
<th>Reason</th>
<th>COPD Exacerbation (n=87)</th>
<th>Non-COPD Hypoventilation (n=35)</th>
<th>Hypoxemic Resp Failure (n=144)</th>
<th>Cardiogenic Edema (n=97)</th>
<th>Post-Ext Failure (n=95)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mask Intolerance</td>
<td>1</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Refractory Hypoxemia</td>
<td>1</td>
<td>43</td>
<td>1</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>Respiratory Acidosis</td>
<td>8</td>
<td>4</td>
<td>8</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>Depressed Mental Status</td>
<td>5</td>
<td>5</td>
<td>11</td>
<td>1</td>
<td>5</td>
</tr>
<tr>
<td>Secretion Accumulation</td>
<td>2</td>
<td>2</td>
<td></td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>Abdominal Distention</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vomiting/Aspiration</td>
<td></td>
<td>1</td>
<td></td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Severe Arrhythmia</td>
<td></td>
<td>2</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Hemodynamic Instability</td>
<td></td>
<td>7</td>
<td>3</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Cardio-resp Arrest (Risk For)</td>
<td>4</td>
<td>3</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Surgical Procedure</td>
<td>1</td>
<td>5</td>
<td></td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Other/Unknown</td>
<td>2</td>
<td>1</td>
<td>5</td>
<td>2</td>
<td>5</td>
</tr>
<tr>
<td>Total Intubate</td>
<td>21</td>
<td>13</td>
<td>87</td>
<td>17</td>
<td>38</td>
</tr>
<tr>
<td>(% intubated)</td>
<td>(24%)</td>
<td>(37%)</td>
<td>(60.4%)</td>
<td>(17.5%)</td>
<td>(40%)</td>
</tr>
</tbody>
</table>

Antonelli CCM 2007;35:18

- 3 ICU survey, NPPV first line Rx ARDS within the first 24 hrs of ICU admission
- 147 with ARDS received NPPV
- 79 (54%) avoided intubation
- Mortality of intubated patients 38 (54%) vs. 15(19%) p <0.01
- ICU length of stay 6 (3-11) success vs. 7 (3-18), p = 0.24
- Severe sepsis 6 (7) vs. 16 (23) p = 0.01
- VAP 2 (2) vs. 14 (20) p = 0.001
NPPV Hypoxemic RF

- Key word is **Caution**!
- Hypoxemic Respiratory Failure in:
  - Post operative Respiratory Failure - **Yes**
  - Immunosuppressed Patients - **Yes**
  - Patients Awaiting Transplantation - **Yes**
  - Patients Post Lung Resection - **Yes**
- Acute Lung Injury – **With Caution**
- Community Acquired Pneumonia – **With Caution**
- Acute Respiratory Distress Syndrome - ????

Elective Extubation to NPPV

- COPD, failed T-piece trial 48-72 hr after intubation
- Randomized to PSV vs. extubation to NPPV
- Better outcome NPPV
  

- No difference in outcome
  
  Girault AJRCCM 1999;160:86

- Failed weaning trial 3 consecutive days, 50% of patients COPD, better outcome NPPV
  
  Ferrier AJRCCM 2003;168:70
Pass SBT - High Risk of Reintubation

- COPD, CHF, ineffective cough and excessive secretions, ≥ one weaning failure, more than one comorbid condition or upper airway obstruction:
  Nava CCM 2005;33:2465
- Age > 65, Cardiac failure cause of intubation or APACHE II > 12 day of extubation:
  Ferrer AJRCCM 2006;173:164
- NPPV > 8 hrs/day for 48 hrs (Nava) or NPPV 24 hrs (Ferrer)
- NPPV less reintubation (both), less ICU/Hosp mortality (Ferrer)

![Graph showing time from extubation to respiratory failure after extubation (hours)]

Ferrer AJRCCM 2006;173:164
NPPV Post-Extubation Failure

- Weaned non-COPD patients developing acute hypoxemic respiratory failure < 48 hours after extubation (n=81)
  - Reintubation rate 72% vs. 69%, LOS, mortality no difference
  - Keenan JAMA 2002;287:3238
- Primarily patients developing acute hypoxemic respiratory failure (n=244), 37 centers, 8 countries
  - Reintubation 48% both groups
  - ICU mortality 25% NPPV vs. 14% p=0.048
  - Time to intubation 12 hr NPPV vs. 2.5 hr p=0.02
  - Esteban NEJM 2004;350:2452

NPPV and Weaning

- Failed weaning NPPV bridge to spontaneous breathing
  - COPD only
- Weaned successfully but high probability of failure
  - COPD, CHF, etc
- Extubation Failure
  - COPD, CHF - Yes
  - Acute Hypoxemic RF - No
Categorization of Indications for NPPV

- Life Support Without Preset Limits
- Life Support With Preset Limits
  - DNI
- Comfort Measures Only
  - DNI

Curtis CCM 2007;35:932

Goals of Therapy

- Category 1 - Improved oxygenation and ventilation, discomfort outweighed by potential benefit!
- Category 2 - To restore health without using endotracheal intubation and without causing unacceptable discomfort!
- Category 3 - Maximize comfort while minimizing adverse efforts of opiates!

Curtis CCM 2007;35:932
Diagnosis and Hospital Outcome:
DNI/DNR patients receiving NPPV

Overall mortality = 64.9%

n= 57  n= 13  n= 10  n= 31  n= 26

Schettino CCM 2005;33:1976
What Do Patients Want!

- Data on patients' perspective of “end of life” based on the experience of cancer patients.
- Primary concern is “loss of autonomy over the circumstances of their dying”.
- Feeling powerless over decisions about medical treatment prolonging life.
  - Simonds Chron Respir Dis 2004;1:56
- The fear of death is being replaced by “the fear of dying”.
  - Clark BMJ 2003;327:174

A Good vs. Bad Death

- A Bad Death: A lack of opportunity to
  - Plan ahead
  - Arrange personal affairs
  - Decrease family burden
  - To say good bye
- A Good Death
  - Pain and symptom management
  - Clear decision making
  - Preparation for death
  - Contributing to others
  - Steinhauser Ann Intern Med 2000;132:825
- Quill. “You promised me I would not die like this” Arch Intern Med 1995;155:1250
  - A Bad Death is a Medical Emergency!
Ethical Dilemma

- Has the patients provided informed consent?
- Ideally, discussions regarding end of life should occur as the patients condition begins to change to provide the patient time to contemplate DNI status and the use of NPPV
- Discussions should occur long before patients are admitted in acute failure
- Patients preferences should be clearly documented in the medical record

NPPV –DNI/DNR

- Does reverse acute RF in many patients
- Does allow patient to communicate and make decisions
- May decrease use of opioids and improve patient comfort?
- Does require that patients be fully informed of what NPPV is and what it is intended to do!
- Add “Do Not Noninvasively Ventilate” to the list of status decisions patients make upon admission
CO₂ rebreathing with the Helmet during CPAP
Lung model and 8 volunteers
CPAP established by:
- ICU ventilator
- 10 L/min contineous flow
- 30 L/min contineous flow
- 60 L/min contineous flow
Taccone CCM 2004;32:2090

Data from 8 Volunteers

<table>
<thead>
<tr>
<th></th>
<th>$V_T^*$</th>
<th>MV*</th>
<th>RR</th>
<th>$P_{iCO_2}^*$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>592+220</td>
<td>5.7+2.0</td>
<td>10+3</td>
<td>0+0</td>
</tr>
<tr>
<td>60 L/min</td>
<td>684+223</td>
<td>6.7+1.4</td>
<td>10+3</td>
<td>2.5+1.3</td>
</tr>
<tr>
<td>30 L/min</td>
<td>789+364</td>
<td>8.3+3.4</td>
<td>11+3</td>
<td>4.6+1.9</td>
</tr>
<tr>
<td>10 L/min</td>
<td>935+441</td>
<td>10.0+3.9</td>
<td>11+4</td>
<td>13.7+6.6</td>
</tr>
<tr>
<td>Ventilator</td>
<td>1020+595</td>
<td>9.0+2.6</td>
<td>9+4</td>
<td>12.4+3.2</td>
</tr>
</tbody>
</table>

* $p < 0.05$

Antonelli Anes 2004;100:16

- Helmet (n = 33) vs. Face mask (n = 33) historical control comparison
- 10 pt Helmet, 14 face mask intubated, $p = 0.22$
- All pts tolerated the Helmet, 6 did not tolerate the Face mask, $p = 0.047$
- At 1 hour $pCO_2$ decreased less with the Helmet (75+15 vs. 66+15) $p = 0.01$
- At D/C of ventilation $pCO_2$ was higher, $p = 0.002$ and pH lower $p = 0.02$ with Helmet
- Complications: Helmet 1, Face mask 12, $p = 0.001$ (skin breakdown 4, conjunctivitis 2 Face mask, DVT Helmet)
### Facial Appliance

<table>
<thead>
<tr>
<th></th>
<th>Nasal</th>
<th>Face</th>
<th>Helmet</th>
<th>Pillows</th>
<th>Total FM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ventilation</td>
<td>++</td>
<td>+++</td>
<td>+</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>Claustrophobia</td>
<td>++</td>
<td>+++</td>
<td>++</td>
<td>+</td>
<td>+++</td>
</tr>
<tr>
<td>Ability to speak</td>
<td>+++</td>
<td>+</td>
<td>++++</td>
<td>+++</td>
<td>++</td>
</tr>
<tr>
<td>Ability to cough</td>
<td>+++</td>
<td>+</td>
<td>++++</td>
<td>+++</td>
<td>++</td>
</tr>
<tr>
<td>Air Leak</td>
<td>+++</td>
<td>++</td>
<td>+</td>
<td>+++</td>
<td>+</td>
</tr>
<tr>
<td>Dead Space</td>
<td>++</td>
<td>++</td>
<td>++++</td>
<td>+</td>
<td>+++</td>
</tr>
<tr>
<td>Comfort</td>
<td>++</td>
<td>+</td>
<td>+++</td>
<td>+++</td>
<td>++</td>
</tr>
</tbody>
</table>

### Humidification

- Essential in acute application of NPPV
- High flows and high F₁O₂ result in dried retained secretions
- Use heated pass over humidifier
- System temperature about 30 degrees C
- Adjust to patient comfort
- Question the use of an HME because of high gas flow and air leak!!!
Ventilator Settings

- PEEP - initially zero
- Peak pressure - 5 cmH₂O
- Volume - 100-200 mL
- Adjust the ventilator from these basic settings based on the patient's response and the goals of therapy!
- Strap the mask only when the patient is comfortable!

Ventilator Settings

- PEEP 3-8 cmH₂O to offset auto-PEEP
- Peak pressure ≤ 20 cmH₂O
- Tidal Volume  300-500 mL
- Inspiratory time < 1.0 sec
- Gastric opening pressure 20-25 cmH₂O
Heliox, NPPV, COPD
N=19 acute exacerbation
70/30 Heliox vs 30% O₂
Heliox improved
- Dyspnea
- PaCO₂
- PaO₂
Jaber AJRCCM 2001; 161:1191

- Heliox, NPPV, COPD
- N=10 acute exacerbation
- 75% to 60% He vs 75% to 60% N₂
- PSV 9 ± 2 and 18 ± 3 cmH₂O
- Heliox improved
  - Patient effort: WOB, PDI, PTP
  - Gas exchange?
RCT - COPD ICU patients receiving NPPV with or without Heliox all ventilator settings same
- 123 pts, 71+10 yrs,
- Intubation rate 20% vs 13% Heliox
- LOS ICU 6.2±5.6 vs 5.1±4 Heliox
- LOS Hosp 19+12 vs 13+6 Heliox p<0.5
- Hosp cost lower by $3,348/pt with Heliox

Heliox enhanced lung emptying in 23 intubated non-spontaneously breathing COPD patients
- Trapped lung volume decreased 116 ml (54%)
- autoPEEP decreased 4 cm H₂O (45%)
- Peak airway pressure decreased 5 cmH₂O (17%)
23 intubated and sedated/paralyzed COPD patients receiving Heliox

WOB decreased with Heliox
2.34±1.04 J/L to 1.85±1.01 J/L, 
p < 0.001

autoPEEP level and inspiratory resistance also decreased!
Jolliet ICM 2003;29:1442

- 10 patients with COPD, invasively ventilated, sedated/paralyzed
- Studied the effect of Heliox and PEEP on autoPEEP
- Heliox and PEEP equally reduced trapped gas (215 ml) and autoPEEP (4.4 cmH$_2$O)
- Heliox also reduced inspiratory and expiratory resistance and plateau pressure

Diehl CCM 2003;31:1415

- COPD patients weaning
- Heliox vs O$_2$/N$_2$ for 20 min before extubation, effect on Work of breathing
- In both situation 29+4% O$_2$ administered
- No modification of the ventilatory pattern
- But Heliox reduced:
  - WOB $1.44\pm0.72$ vs $1.13\pm0.50$ J/L
  - $\text{PEEP}_A$ $2.9\pm2.1$ vs $2.2 \pm1.8$
Who – Indications for NPPV

**Undisputed indications**
- Acute Exacerbation of COPD
- Acute Cardiogenic Pulmonary Edema

**General Indications for Use**
- Post extubation Hypercarbic Respiratory Failure
- Hypoxemic Respiratory Failure in:
  - Immunosuppressed Patients
  - Patients Awaiting Transplantation
  - Patients Post Lung Resection
- Patients with DNI Status
- Acute Hypercapnic Respiratory Failure as a Result of Neurological or Neuromuscular Disease

**Controversial Indications**
- Post –Extubation Hypoxemic Respiratory Failure
- Acute Lung Injury
- Acute Respiratory Distress Syndrome
- Asthma

Thank You