NIPPV in non COPD acute respiratory failure– current status and recent advances

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Introduction

- Noninvasive ventilation is the delivery of ventilatory support without the need for invasive artificial airway

- Based on the results of clinical trials showing improved outcomes in certain types of acute respiratory failure its use has ↑ed in recent years

Am J Respir Crit Care Med 2001; 163:540–577

Types of Noninvasive Ventilation (NIV)

- Negative Pressure Ventilation (NPV)
- Continuous Positive Airway Pressure (CPAP)
- Noninvasive Positive Pressure Ventilation (NPPV)

Negative Pressure Ventilation

- Negative pressure ventilators apply a negative pressure intermittently around the patient's body or chest wall → iron lung or tank ventilator

- Pressure is applied intermittently to the thoracic area resulting in a pressure drop around the thorax

- Negative pressure is transmitted to the pleural space and alveoli creating a pressure gradient between the inside of the lungs and the mouth

- As a result gas flows into the lungs

Continuous Positive Airway Pressure - CPAP

- Form of noninvasive support usually applied through a mask-type device

- Does not
  - provide volume change
  - Support patient's minute ventilation

- Often used for two different clinical situations
  - Therapeutic technique for treating OSA pt
  - Acute care facility to help improve oxygenation -> patients with acute congestive heart failure

Noninvasive Positive Pressure Ventilation

- NPPV provides positive pressure through the upper airway by some type of mask or other noninvasive interface
- Provision of inspiratory pressure support plus PEEP & is used to treat both acute and chronic respiratory failure
- In acute care setting NPPV → treat patients with acute respiratory failure
- In chronic respiratory failure→ used to provide 24-hour ventilatory support

- IPAP
  - Augments tidal volume
  - Increases airway pressure
  - Decreases fatigue

- EPAP splint and maintains a fixed alveolar pressure
  - Prevents airway and alveolar collapse
  - Prevents atelectasis
  - Maintains functional residual capacity at increased levels
  - It maintains oxygenation

NIV - evidence

Table 1. Noninvasive ventilation for various types of acute respiratory failure (ARF): Evidence for efficacy and strength of recommendation

Type of ARF	Level of Evidence[a]	Strength of Recommendation[b]
Hypercapnic respiratory failure		
COPD exacerbation	A	Recommended
Asthma	C	Option
Facilitation of extubation (COPD)	A	Guideline
Hypoxemic respiratory failure		
Cardiogenic pulmonary edema	A	Recommended
Pneumonia	C	Option
ALI/ARDS	C	Option
Immunocompromised	A	Recommended
Postoperative respiratory failure	B	Guideline
Extubation failure	C	Guideline
Do not intubate status	C	Guideline
Preintubation oxygenation	B	Option
Facilitation of bronchoscopy	B	Guideline

COPD, chronic obstructive pulmonary disease; ALI, acute lung injury; ARDS, acute respiratory distress syndrome.

[a]A, multiple randomized controlled trials and meta-analyses; B, more than one randomized, controlled trial, case control series, or cohort studies; C, case series or conflicting data; [b] recommended, first choice for ventilatory support in selected patients; Guideline, can be used in appropriate patients but careful monitoring advised; Option, suitable for a very carefully selected and monitored minority of patients.

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Hypercapnic Respiratory Failure

NIV should be considered first-line therapy in the management of ARF due to COPD exacerbations based on evidence derived from multiple randomized trials

N Engl J Med 1990; 323: 1523–1530

*Lancet 1993;*341:1555–1557

Am J Respir Crit Care Med 1995; 151:1799–1806

NIV - Asthma

- Acute asthmatic attacks similar to exacerbations of COPD are characterised by
  - increase in inspiratory and expiratory indexes of airway obstruction
  - significant dynamic hyperinflation
  - generation of a large negative pleural pressure needed to overcome the increased end-expiratory intrathoracic pressure and airway resistance

- Progressive decline in FEV_1 leads to proportional increase in the inspiratory work of breathing → inspiratory muscle fatigue

- Increased physiologic dead space and ventilation perfusion mismatch lead to worsening hypoxemia with hypercarbia and respiratory failure

NIV - Asthma

- CPAP has
  - bronchodilatory effect
  - unload fatigued inspiratory muscles
  - improve gas exchange
  - prevents methacholine and histamine-induced asthma

- Noninvasive ventilatory support
  - increases tidal volume
  - Adds external PEEP to offset the intrinsic PEEP that builds up during an asthmatic attack → decreasing the work of the inspiratory muscles

NIV - Asthma

- Evidence is weaker for the use of NIV in asthma patients with acute respiratory failure

- An uncontrolled study - improved gas exchange and intubation avoided 15 of 17 patients with status asthmaticus & 100% survival

- NIV using face mask was effective in
  - correcting gas exchange abnormalities at lower inspiratory pressures (< 25 cm H2O)
  - preventing tracheal intubation

Meduri GU et al. Chest 1996

NIV - Asthma

- Randomized pilot study in 33 patients with acute asthma showed improved flow rates and decreased hospitalizations with NIV vs. sham NIV

- NPPV using low inspiratory pressures (< 15 cm H2O) was highly effective in
  - rapidly improving lung function
  - respiratory rate
  - decreasing hospitalization

- NIV shuold be restricted to carefully selected cases with optimal medical management & routine clinical use in Ac severe asthma not recommended

Soroksky et al. Chest 2003

NIV - Asthma

- A trial of NIV can be considered in asthmatics who fail to respond adequately to initial bronchodilator therapy to
  - improve air flow obstruction
  - decrease the work of breathing

- Patients should be monitored closely and intubated promptly if there is no improvement in the first hour or two

- According to the BTS Standards of Care Committee Statements: ‘‘NPPV should not be used routinely in acute asthma, but a trial might be considered in patients not promptly responding to standard treatments’’

Thorax 2002; 57: 192–211

NIV - Asthma

A prospective RCT on the efficacy of NIV in SAA

- 53 patients were randomized to NIV (n=28) and SMT (n=25)
- Median IPAP and EPAP used was 12 and 5 cm H_2O respectively
- Significant improvement in RR, FEV_1 and PaO_2-FiO_2 (but not pH and $PaCO_2$) in both the groups but not between the two groups
- Patients achieving a 50 % improvement in FEV_1 at one, two and four hours were greater in the NIV arm, but statistically insignificant

Agarwal R et.al submitted for publication

NIV - Asthma

- Length of ICU and hospital stay & mean doses of inhaled bronchodilators were significantly lesser in the NIV group
- 4 instances of SMT failure and all these patients improved with NIV
- Two patients in the NIV arm required invasive ventilation & no mortality in either of the arms
- Study concluded that addition of NIV to SMT is
  - likely to accelerate the improvement in lung function with requirement of lower doses of inhaled bronchodilators
  - shorten the ICU and hospital stay in patients with acute severe asthma

Agarwal R et.al submitted for publication

NIV - Asthma

- Cochrane systemic review - application of NPPV in patients suffering from status asthmaticus, despite some interesting and very promising preliminary results, still remains controversial

- Large, prospective, randomised controlled trials are needed to determine the role of NPPV in status asthmaticus

Rowe BH et al. Cochrane Database Syst Rev 2005

NIV-Weaning

Facilitating Extubation in COPD

- Supported by strong evidence

- RCT in patients with COPD and hypercapnic respiratory failure who failed a single / repeated T-piece trials → extubated to NIV or continued on invasive ventilation and weaned according to a standard pressure support protocol

  - an increased weaning rate at 28 days
  - decreased durations of MV and ICU stay
  - reduced rates of nosocomial pneumonia and 60-day mortality

Ferrer M et al. Am J Respir Crit Care Med 2003

NIV-Weaning

Conclusion

- patients intubated for hypercapnic respiratory failure due to COPD who fail SBT should be considered for a trial of extubation to NIV

- Approach should be reserved for patients who are
  - Good candidates for NIV
  - Able to tolerate levels of pressure support easily administered via mask (i.e., 15 cm H_2O)

- Should not have been a difficult intubation

NIV-Weaning

- Experimental RCT followed up 65 patients undergoing IMV for > 48 hours & who failed a spontaneous breathing T-piece trial

- During the trial, RR, TV, minute volume, rapid shallow breathing index, HR, ABP, & SpO_2 were measured at 1 and 30 minutes

- After failing a T-piece trial, patients were randomly divided in two groups
  - Extubated and placed on NPPV (n=28)
  - Returned to IMV (n=37)

Trevisan *et al. Critical Care 2008*

NIV-Weaning

- HD, post-surgery RF, & COPD aggravation were the most frequent causes of IMV use
- NPPV group had lower
  - % age of complications (28.6% versus 75.7%)
  - incidences of pneumonia /tracheotomy

- Length of stay in the ICU and mortality not statistically different with in groups

- Suggest that NPPV is a good alternative for ventilation of patients who fail initial weaning attempts & it reduces the incidence of pneumonia & the need for tracheotomy

Trevisan *et al. Critical Care 2008*

Meta-analysis of noninvasive weaning to facilitate liberation from mechanical ventilation

Study Year (n)	*Eligibility criteria*	*Inclusion criteria*	*Exclusion criteria*	*Interventions*		*Outcomes reported*
				Extubation and NPPV	*IPPV*	
Nava 1998 (50)	COPD (AE) MV > 36–48 hr pH ≤ 7.33 Elevated bicarbonate PaO_2 ≤ 45 mmHg Severe dyspnea No other etiology	Permissive criteria Failure of a 1-hr T-piece trial	Cardiac arrest Cardiogenic edema Aortic aneurysm Neurologic diseases Cancer Myocardial infarction GI perforation Postoperative Sepsis Trauma Coagulopathy	PS mode with face mask Initial PS set to achieve prior $PaCO_2$, pH, RR < 25 to 30 beats·min^{-1} and satisfactory ABGs PS delivered 20–22 hr·day^{-1} during first 48 hr separated by periods of SB with supplemental oxygen PS decreased by 2 to 4 cm H_2O·day^{-1} with at least 2 periods of SB·day^{-1} of increasing duration Discontinued: criteria + successful 3 hr SB period	Initial PS set to achieve prior $PaCO_2$ and pH and RR < 30 beats·min^{-1} PS titrated to RR < 25 beats·min^{-1} and SBT performed twice daily using T-piece or CPAP < 5 cm H_2O Discontinued: criteria + successful 3 hr SBT	60-day mortality Successful weaning at 60 days Incidence VAP Total duration of MV in ICU ICU length of stay Adverse events Tracheostomy
Girault 1999 (33)	ACRF Obstructive and restrictive difficult to wean MV ≥ 48 hr	Screening after 48 hr MV Permissive criteria Failure of a 2-hr T-piece trial	Ineffective cough Difficult intubation Swallowing disorder Bronchial congestion Lack of cooperation Recent GI surgery Intestinal ileus	PS or flow mode delivered by face or nasal mask EPAP adjusted to offset iPEEP NPPV delivered intermittently separated by at least 2 periods of SB·day^{-1} of gradually increasing duration starting at 1–2 hr At least 2 periods of observation per day Discontinued: physician observation of SB	Initial PS set to maintain RR 20 to 30 beats·min^{-1} with initial flows 0.1–0.25 sec PEEP to offset iPEEP PS titrated by 3–5 cm H_2O according to tolerance At least 2 periods of observation per day Discontinued: physician observation of 2 periods of decreased PS Extubation permitted when PS ≤ 8 cm H_2O	90-day mortality Hospital mortality Successful weaning Incidence VAP Duration MV related to weaning Duration of ETMV Mean daily period of support ICU length of stay Hospital length of stay Adverse events Reintubation Tracheostomy
Chen 2001 (24)	COPD (AE) pH ≤ 7.35 PaO_2 ≤ 45 torr RR > 30 beats·min^{-1} MV > 48–60 hr	Permissive criteria	NA	PS mode titrated to RR and ABGs Gradual decrease in PS and PEEP Discontinued: criteria + successful 3 hr SB period	Initial PS titrated to RR and ABGs Gradual decrease in PS and PEEP Discontinued: criteria + successful 3 hr SBT	Mortality Incidence VAP Duration MV related to weaning Hospital length of stay
Ferrer 2003 (43)	ARF Persistent weaning failure MV > 72 hr	Daily screening Permissive criteria Failure of 2 hr T-piece trial on 3 consecutive days	Cranial/facial trauma or surgery Recent gastric or esophageal surgery Tracheotomy Upper GI bleeding Excessive secretions Lack of cooperation	Bilevel ventilation in ST mode delivered continuously during first 24 hr Periods of SB of gradually increasing duration	AC or PS titrated at physician discretion Daily T-piece trials until extubation Discontinued: after successful 2 hr SBT	ICU mortality, 90-day mortality Incidence VAP Duration MV related to weaning Duration of ETMV Total duration of MV ICU length of stay Adverse events Reintubation Tracheostomy
Hill* 2000 (21)	ARF Not restricted to COPD	Daily screening Failure of 30-min T-piece trial	Excessive secretions Difficult intubation Unable to tolerate PS < 15 cm H_2O Unable to breathe spontaneously	VPAP – PS in ST mode by face and nasal mask delivered continuously Titrated to RR and V_T At least one period of SB/d of gradually increasing duration	PS titrated to RR and V_T T-piece trials permitted	Mortality Successful weaning Duration of ETMV Reintubation

COPD = chronic obstructive pulmonary disease; AE = acute exacerbation; ACRF = acute on chronic respiratory failure; ARF = acute respiratory failure; MV = mechanical ventilation; PaO_2 = arterial partial pressure of oxygen; $PaCO_2$ = arterial partial pressure of carbon dioxide; GI = gastrointestinal; NPPV = noninvasive positive pressure ventilation; IPPV = invasive positive pressure ventilation; AC = assist control; PS = pressure support; RR = respiratory rate; V_T = tidal volume; CPAP = continuous positive airway pressure; VPAP = ventilator (delivered) positive airway pressure; ST = spontaneous timed; SBT = spontaneous breathing trial; SB = spontaneous breathing; ABGs = arterial blood gases; VAP = ventilator associated pneumonia; ETMV = endotracheal mechanical ventilation; NA = not available; ICU = intensive care unit; PEEP = positive end-expiratory pressure; EPAP = intermittent positive end-expiratory pressure; iPEEP = expiratory positive airway pressure. *Trial published in abstract form only. To convert torr to kPa, multiply by 0.13333.

Karen EA et al.CAN J ANESTH, 2006

NIV-Weaning

- 5 studies enrolling 171 patients demonstrated that compared to IPPV, noninvasive weaning decreased
  - mortality (relative risk, 0.41 [95% confidence interval [CI] 0.22–0.76]),
  - VAP(relative risk, 0.28 [95% CI 0.09–0.85]) and
  - Total duration of MV (weighted mean difference, -7.33 days [95% CI -11.45 to -3.22 days]).

- Conclusions –
  - Noninvasive weaning demonstrated a consistent positive effect on mortality
  - NPPV to facilitate weaning with predominantly COPD, is associated with promising, but insufficient, evidence of net clinical benefit

Karen EA et al. CAN J ANESTH, 2006

Hypoxemic Respiratory Failure

- Hypoxemic ARF is defined by a PaO_2/ FIO_2 ratio < 300 while breathing oxygen through venturi mask and a variety of different non-COPD etiologies

NIV-CPE

- Use of NIV or CPAP in patients with CPE is supported by multiple RCT

- Physiologic benefit from NIV or CPAP in these patients is likely due to
  - increase in FRC that reopens collapsed alveoli and improves oxygenation → increases lung compliance and reduces work of breathing
  - increased intrathoracic pressure leading to improve cardiac performance by decreasing ventricular preload and afterload

- Meta-analyses have shown equivalent reductions in intubation and mortality rates with CPAP and NIV

JAMA 2005; 294:3124–3130
Crit Care 2006; 10:R69

Table. Randomized Studies Analyzing Noninvasive Ventilation

Source	Location	Sample Size*	Mask	CPAP, cm H_2O	IPAP/EPAP, cm H_2O	Primary Outcomes	Other Considerations
Continuous Positive Airway Pressure vs Oxygen Therapy							
Räsänen et al,[3] 1985	1 ICU in Finland	40	Full face	10		Clinical outcomes	
Bersten et al,[4] 1991	1 ICU in Australia	40 (39)	Full face	10		Intubation	
Lin et al,[5] 1995	1 ICU in Taiwan	100	Full face	2.5-12.5		Intubation In-hospital mortality	Swan-Ganz catheterization
Takeda et al,[29] 1997	1 ICU in Japan	30 (29)	Full face or nasal	4-10		Laboratory parameters	Measurement of plasma endothelin 1
Kelly et al,[31] 2002	1 ED and ICU in the United Kingdom	58	Full face	7.5		Clinical outcomes Laboratory parameters	Measurement of plasma neurohormonal concentrations
L'Her et al,[7] 2004	4 EDs in France	89	Full face	7.5		48-h mortality	Elderly patients (>75 y)
Noninvasive Pressure Support Ventilation vs Conventional Oxygen Therapy							
Masip et al,[9] 2000	1 ICU in Spain	40 (37)	Full face		20/5, Mean	Intubation Resolution time	IPAP was adjusted to tidal volume
Levitt,[33] 2001	1 ED in the United States	38	Full face or nasal		8/3 Initial	Intubation	Prematurely interrupted when the study by Mehta et al[35] was published
Nava et al,[34] 2003	5 EDs in Italy	130	Full face		14.5/6.1, Mean	Intubation	Post hoc analysis in hypercapnic patients
Trials With 3 Study Groups							
Park et al,[30] 2001	1 ED in Brazil	26	Full face and nasal	5-12.5	8/3 Initial	Intubation	Full-face mask for CPAP and nasal for NIPSV
Crane et al,[32] 2004	2 EDs in the United Kingdom	60	Full face	10	15/5 Fixed	Success in ED (2 h) In-hospital mortality	Prehospital nitrates therapy evaluated
Park et al,[8] 2004	1 ED in Brazil	83 (80)	Full face	10 Initial up to 16	15/10 Initial	Intubation	
Continuous Positive Airway Pressure vs Noninvasive Pressure Support Ventilation							
Mehta et al,[35] 1997	1 ED in the United States	27	Nasal and full face	10	15/5 Fixed	Intubation Physiological improvement	Prematurely stopped for higher rate of AMI in NIPSV group
Bellone et al,[36] 2004	1 ED in Italy	36	Full face	10	15/5 Initial	AMI	Study restricted to patients with hypercapnia
Bellone et al,[37] 2005	1 ED in Italy	46	Full face	10	15/5 Initial	Resolution time	Primary end point was AMI rate Only nonischemic APE

Abbreviations: AMI, acute myocardial infarction; APE, acute pulmonary edema; CPAP, continuous positive airway pressure; ED, emergency department; EPAP, positive expiratory airway pressure (equivalent to CPAP); ICU, intensive care unit; IPAP, inspiratory positive airway pressure; NIPSV, bilevel noninvasive pressure support ventilation.
*Numbers in parentheses denote the number of patients finally included after withdrawals.

Masip J et al. *JAMA* 2005

NIV-CPE

- Meta-analysis reviewed short-term effect of NIV on major clinical outcomes

- NIV reduces the need for intubation and mortality in patients with acute CPE

- Although the level of evidence is higher for CPAP, there are no significant differences in clinical outcomes when comparing CPAP vs NIPSV

Masip J et al. *JAMA* 2005

NIV-CPE

- Several studies have shown more rapid reductions in respiratory rate and dyspnea with NIV than with CPAP alone

  Emerg Med J 2004; 21:155–161

- NIV or CPAP can be used to treat CPE with equal success

- Some recommend starting with CPAP, because it is a simpler & potentially less expensive therapy, with pressure support added if patients remain dyspneic or hypercapnic on CPAP alone

NIV-CPE

Metaanalysis including 16 RCT. Concluded that

- NIV improves haemodynamics and respiratory parameters along with conventional treatment
- CPAP decreases intubation rate and improves survival (NNT 7 and 8)
- Decreased use IMV ,shorter ICU stay & hospital stay and reduced mortality in selected cases
- Insufficient evidence for use of BiPAP except hypercapnic CPE
- BiPAP needs further evaluation in CPE

Agarwal R et al. Postgrad Med J 2005

NIV-CPE

- Study to determine whether
  - NIV reduces mortality
  - Important differences in outcome associated with the method of treatment (CPAP or NIPPV)
- Multicenter, open, prospective RCT, patients were assigned
  - standard O_2 therapy,
  - CPAP (5 to 15 cm of water)
  - NIPPV (IPAP, 8 to 20 cm of H_2O; EPAP, 4 to 10 cm of H_2O)
- The primary end point
  - comparison between NIV & standard O_2 therapy was death within 7 days after the initiation of treatment
  - comparison between NIPPV and CPAP was death or intubation within 7 days

N Engl J Med 2008;359:142-51

NIV-CPE

- 1069 patients included. standard oxygen therapy (367 patients), CPAP (346 patients), or NIPPV (356 patients)

- No significant difference in 7-day
  - mortality
  - combined end point of death or intubation between the NIV groups

- NIV was associated with greater mean improvements at 1 hour of treatment in patient-reported
  - Dyspnea, heart rate, Acidosis & Hypercapnia

- Conclusion - in acute CPE , NIV induces a more rapid improvement in respiratory distress and metabolic disturbance than does standard O_2 therapy but has no effect on short-term mortality

N Engl J Med 2008;359:142-51

NIV-CPE

- Systematic review - effectiveness & safety of NIPSV as compared to CPAP in CPE

- 10 studies were included. NIPSV performed similar to CPAP in decreasing
  - intubation rates, hospital mortality & occurrence of myocardial infarction

- Results were similar for the type of pressure therapy (fixed vs. variable) except for myocardial infarction, which was more frequent in the fixed pressure NIPSV arm

- Conclusion - NIPSV appears to be as safe and efficacious as CPAP, if titrated rather than fixed pressures are employed

Agarwal R,Singapore Med J 2009

NIV-CPE : Concrane review

- Data fromRCTs have demonstrated that NPPV(CPAP and bilevel NPPV) is effective in reducing hospital mortality, intubation rate and ICU length of stay

- NPPV resulted in faster improvement and was better tolerated than standard medical care

- Meta-analysis did not demonstrate an increase in the incidence of adverse events or AMI during & after NPPV

Vital FMR et al. Cochrane Database of Systematic Reviews 2008

NIV-CPE : Concrane review

- CPAP should be considered as first option as evidence for BiPAP remains inconclusive due to insufficient patient numbers recruited to the studies to detect statistical power to define its effectiveness

Implications

- Further studies are required to reduce uncertainty regarding length of hospital stay, long-term mortality, costs and the time required to manage NPPV

- Additional research is required to elucidate if
  - hypercapnic patients with ACPE may benefit to a greater extent than non-hypercapnic patients
  - bilevel NPPV confers additional benefit compared to CPAP

Vital FMR et al. Cochrane Database of Systematic Reviews 2008

NIV-pneumonia

- Challenge to treat noninvasively and has been identified as a risk factor for NIV failure

Intensive Care Med 2001; 27: 1718–1728

- Cohort study
  - 2/3rd of patients with severe CAP required intubation
  - Successful NIV had very good outcomes

Intensive Care Med 2001; 27:812–821

- An RCT on patients with severe CAP showed that NIV reduced intubation rates, ICU length of stay, and 2-month mortality rate, but only in the subgroup with underlying COPD

Am J Respir Crit Care Med 1999; 160:1585–1591

NIV-pneumonia

- RCT on patients with hypoxemic respiratory failure showed that NIV reduced the need for intubation among patients with pneumonia (26% vs. 73% in the conventional therapy group)

- Reasons
  - patients from this study were more severely hypoxemic & NIV may be a significantly better support than oxygen therapy alone
  - subset of patients receiving NIV in a previous study were more seriously ill than those from the control group, as assessed by higher APACHE -II score

Ferrer M et al. Am J Respir Crit Care Med 2003

NIV-pneumonia

- RCT testing NIV as an alternative to IMV in patients with various types of ARF found → subgroup with pneumonia did very poorly, with all 8 patients randomized to NIV requiring intubation

Honrubia T et al. Chest 2005

- Scant and conflicting data do not support the routine use of NIV in patients with severe pneumonia, with the exception of patients with underlying COPD

- Cautious trial of NIV may be considered in patients with pneumonia, but they need careful monitoring, because the risk of failure is high

NIV-ALI/ARDS

- Studies on NIV to treat ALI and ARDS have reported failure rates ranging from 50% to 80%

- Independent risk factors for NIV failure in this group of patients include severe hypoxemia, shock, and metabolic acidosis

Crit Care 2006; 10:R79

- Prospective multicenter survey found that when NIV was used as first-line therapy for selected ALI/ ARDS patients (Excluding - 2 organ failures, HD instability, or encephalopathy) 54% avoided intubation and had excellent outcomes

*Crit Care Med 2007; 35:*18–25

NIV-ALI/ARDS

- Predictors of NIV failure were
  - Simplified Acute Physiology Score > 34
  - PaO_2/FIO_2 <175 after the first hour of therapy

- NIV cannot be recommended as routine therapy for ALI/ ARDS but data support a cautious trial in highly selected patients with a
  - Simplified Acute Physiology Score < 34 and
  - Readiness to promptly intubate if oxygenation fails to improve sufficiently within the first hour

NIV-ALI/ARDS

- Meta-analysis : aim to assess the effect of NIV on the rate of endotracheal intubation and ICU mortality

- Addition of NIV to standard care in the setting of ARDS
  - Did not reduce the rate of endotracheal intubation (absolute risk reduction (RR) 13.5%, 95% confidence interval (CI) 5.2% to 31.3%)
  - No effect on ICU survival

- Analysis was limited by the presence of significant heterogeneity; hence large randomized controlled trials are required to settle this issue

Agarwal R et al. Respiratory Medicine 2006

NIV-ALI/ARDS

- Prospective observational study to determine the outcomes of NIPPV & factors associated with NIPPV failure in patients with AHRF
- 40 patients - 21- ALI/ARDS & 19- AHRF due to other causes were initiated on NIPPV
- After 1 hour there was a significant ↓in RR & HR with ↑ in pH and PaO_2 levels
- No difference in improvement of clinical and blood gas parameters between the two groups
- NIPPV failures, the mean ICU and hospital stay, and the hospital mortality were similar in the two groups

Agarwal R et al. Respiratory Care 2009. In press

NIV-ALI/ARDS

- Conclusion -NIPPV should be judiciously used in patients with AHRF as failure rate are high (57% in ALI/ARDS group)
- NIPPV offers ventilatory support with an advantage of reduced incidence of nosocomial pneumonia and reduced ICU stay and overall hospital costs
- NIPPV must be applied early and patients monitored closely in intensive care setting so that endotracheal intubation can be carried out without any delay
- A low baseline PaO_2-FiO_2 ratio was associated with NIPPV failure

Agarwal R et al. Respiratory Care 2009. In press

NIV- Immuno-compromised Patients

- RCTs in recipients of solid-organ or bone-marrow transplants who developed hypoxemic respiratory failure have found
  - decreased intubation and ICU mortality rates
  - shorter ICU stay

  in patients treated with NIV as compared with conventional therapy

JAMA 2000; 283:235–241
*N Engl J Med 2001; 344:*481–487

- Similar findings have been reported in a nonrandomized study for AIDS patients

Intensive Care Med 2002; 28:1233–1238

NIV- Immuno-compromised Patients

- The reduced mortality is likely related to reduced infectious complications associated with NIV use compared with endotracheal intubation
  - VAP
  - Other nosocomial infections
  - Septic shock

*Intensive Care Med 1999; 25:*567–573

- Data support NIV as the preferred initial ventilatory modality to avoid intubation and its associated risks

NIV-Postoperative Respiratory Failure

- Benefit in the postoperative period when used prophylactically after major abdominal surgery or thoracoabdominal aneurysm repair

- CPAP (10 cm H2O) reduces the incidence of hypoxemia, pneumonia, atelectasis, and intubations compared with standard treatment

- Only RCT of NIV in the postoperative setting, patients with hypoxemic respiratory failure after lung resection had reduced intubation and mortality rates compared to standard management

Respir Crit Care Med 2001; 164:1231–1235

NIV- PERF

- Evidence-based guidelines recommend a SBT to determine whether mechanical ventilation can be successfully discontinued & with this approach, the documented need for reintubation ranges from 13 to 19 %

Am J Respir Crit Care Med 1999;159:512-8

- Extubation failure is associated with high morbidity and mortality

- NIV has been suggested as a way to avoid re-intubation and improve outcomes

NIV- PERF

- RCT found no reduction in reintubations among patients who developed respiratory distress within 48 hrs of extubation
  - Few COPD patients included
  - Pressure support used may have been subtherapeutic

Keenan SP et al. JAMA 2002

- RCT attempted to prevent extubation failure by starting NIV / ST as soon as patients developed signs of extubation failure

- NIV fail to reduce reintubations & was associated with increased ICU mortality - related to delays in needed reintubation

- Only 10% of patients in this trial had COPD

Esteban A et al. N Engl J Med 2004

NIV- PERF

- Two RCTs involving pt at high risk for extubation failure found that NIV reduced the need for reintubation and ICU mortality & hypercapnic subgroup were most benefited

Ferrer M et al. Am J Respir Crit Care Med 2006

- Data support the use of NIV in patients at high risk of extubation failure → COPD / CHF / hypercapnia

- Concluded : early indiscriminate use in all patients with risk factors is discouraged & monitored closely to avoid needed intubation

NIV- PERF

- Meta-Analysis - 4 studies were included, 2 each for established PERF & “at risk” for PERF

- NPPV, compared to the SMT in PERF did not decrease the
  - Re-intubation rate /ICU mortality

- High risk for developing PERF, NPPV decreased
  - Re-intubation rate /ICU mortality
    but not the hospital mortality

- Conclusion:
  - NPPV should be used judiciously, if at all, in patients with PERF
  - promising as a prophylaxis to prevent re-intubation in patients “at risk” for developing PEFR

Agarwal R et al. Respir Care 2007

Table 4. Practical Approach to the Use of NPPV in the Postextubation Setting

NPPV in Patients At Risk for Postextubation Respiratory Failure
(Preferred approach for the use of NPPV in the postextubation setting)
Identify high-risk features
Elderly patients (age > 65 y)
More than one consecutive failure of weaning trial
Chronic heart failure
P_{aCO_2} > 45 mm Hg after extubation
More than one medical/surgical co-morbid illness
Poor cough reflex
Upper-airways stridor at extubation that does not require immediate reintubation
APACHE II score > 12 on the day of extubation
Severely obese patients (body mass index > 35 kg/m^2)
NPPV in Established Postextubation Respiratory Failure
Use judiciously
Likely to benefit selected patients (eg, acute COPD, hypercapnic pulmonary edema)
Trial of NPPV for 2 hours
Close monitoring of respiratory, cardiovascular and arterial blood gas variables
Facilities for intubation and invasive ventilation readily available

NPPV = noninvasive positive-pressure ventilation
APACHE - Acute Physiology and Chronic Health Evaluation
COPD = chronic obstructive pulmonary disease

Agarwal R et al. Respir Care 2007

NIV- Palliative Care and Do-Not-Intubate Status

- Prospective cohort series of 114 patients with acute respiratory failure and a status of do not intubate
- 43% of the patients survived the hospitalization
- CPE & COPD had hospital survival rates 50%
- Presence of a cough and an awake mental status had favorable prognosis

Levy MM et al. Crit Care Med 2004

NIV- Palliative Care and Do-Not-Intubate Status

- Prospective cohort series showed
  - favorable success rates in do not intubate patients with COPD and CPE
  - high failure rate in patients with hypoxemic respiratory failure / post-extubation failure / end-stage cancer

Schettino G,Crit Care Med 2005

- Depending on patient and/or family wishes, a trial of NIV can be considered in do-not intubate patients, but the goals of therapy should be clear

Curtis RJ et al. Crit Care Med 2007

NIV- Palliative Care and Do-Not-Intubate Status

Goal of therapy

- If the patient and/or family desire prolonged survival→ use should be reserved primarily for COPD and CHF patients

- If is palliative, to relieve dyspnea, or to delay death so that affairs can be settled then NIV can be used for other diagnoses as well

- Should be reassessed frequently and stopped if the goal of palliation is not being met

NIV - Flail chest

- prospective, randomised study of CPAP via a face mask to compared with IPPV with ETI in 52 patients with flail chest
- Nosocomial infection diagnosed in 10 of 21 patients in the ET group, but only in 4 of 22 in he CPAP group ($p < 0.001$)
- Mean PO_2 was significantly higher in the ET group in the first 2 days but no significant differences in length of ICU stay
- 20 CPAP patients survived, but only 14 of 21 intubated patients who received IPPV ($p < 0.01$)
- study supports the application of CPAP as a first line of treatment for flail chest caused by blunt thoracic trauma

Gunduz M et al. Emerg Med J 2005

NIV - Other ICU Applications

Preoxygenation Before Intubation

- Critically ill patients with AHRF are at high risk of O_2 desaturations during intubation

- RCT of such patients showed that pre-oxygenation with NIV before intubation resulted in
  - improved oxygen saturation during and after intubation
  - decreased the incidence of oxygen desaturations below 80% during intubation

Am J Respir Crit Care Med 2006; 174:171–177

- Approach is promising & needs further studied before routine use can be recommended

NIV- FOB

- RCT has shown that CPAP alone (up to 7.5 cm H2O) improves oxygenation and reduces postprocedure respiratory failure in patients with severe hypoxemia

Am J Respir Crit Care Med 2000; 162:1063–1067

- RCT of 26 patients with hypoxemia ($PaO2/FIO_2$ ratio < 200 NIV
  - increased PaO2/FIO2 by 82%
  - 10% worsening in the conventional O_2 therapy

- NPPV is superior to conventional O_2 supplementation in preventing gas-exchange deterioration during FOB with better hemodynamic tolerance

Chest 2002; 121:1149–1154

NIV- FOB

- Successful bronchoscopy during NIV also has been reported in hypercapnic COPD patients with pneumonia

- NIV improved oxygen saturation, and all 10 patients tolerated the procedure without complications

Ann Fr Anesth Reanim 2000; 19:231–236

- Evidence supports the use of NIV during FOB when risks of intubation are high → immunocompromised / bleeding diatheses

- Be prepared for the possibility of emergent intubation

Conclusion

- Strong evidence from RCT to supports the use of NIV in ARF to prevent endotracheal intubation in pt
  - COPD exac.
  - ACPE
  - Immunocompromised pt.
  - facilitate extubation in COPD pt.

- NIV should be contemplated in patients
  - postoperative respiratory failure
  - high risk for PEFR who are otherwise good candidates for NIV
  - preoxygenating critically ill patients with hypoxemia before intubation

Conclusion

- NIV can be considered in patients
  - asthma exacerbations
  - Pneumonia
  - ALI/ARDS

  supporting evidence is fairly weak
- Patients should be monitored closely for signs of NIV failure until stabilized

- Should be intubated promptly at failure before a crisis develops

- Application of NIV by a trained and experienced ICU team, with careful patient selection, should optimize patient outcomes