NIV in non COPD acute respiratory failure

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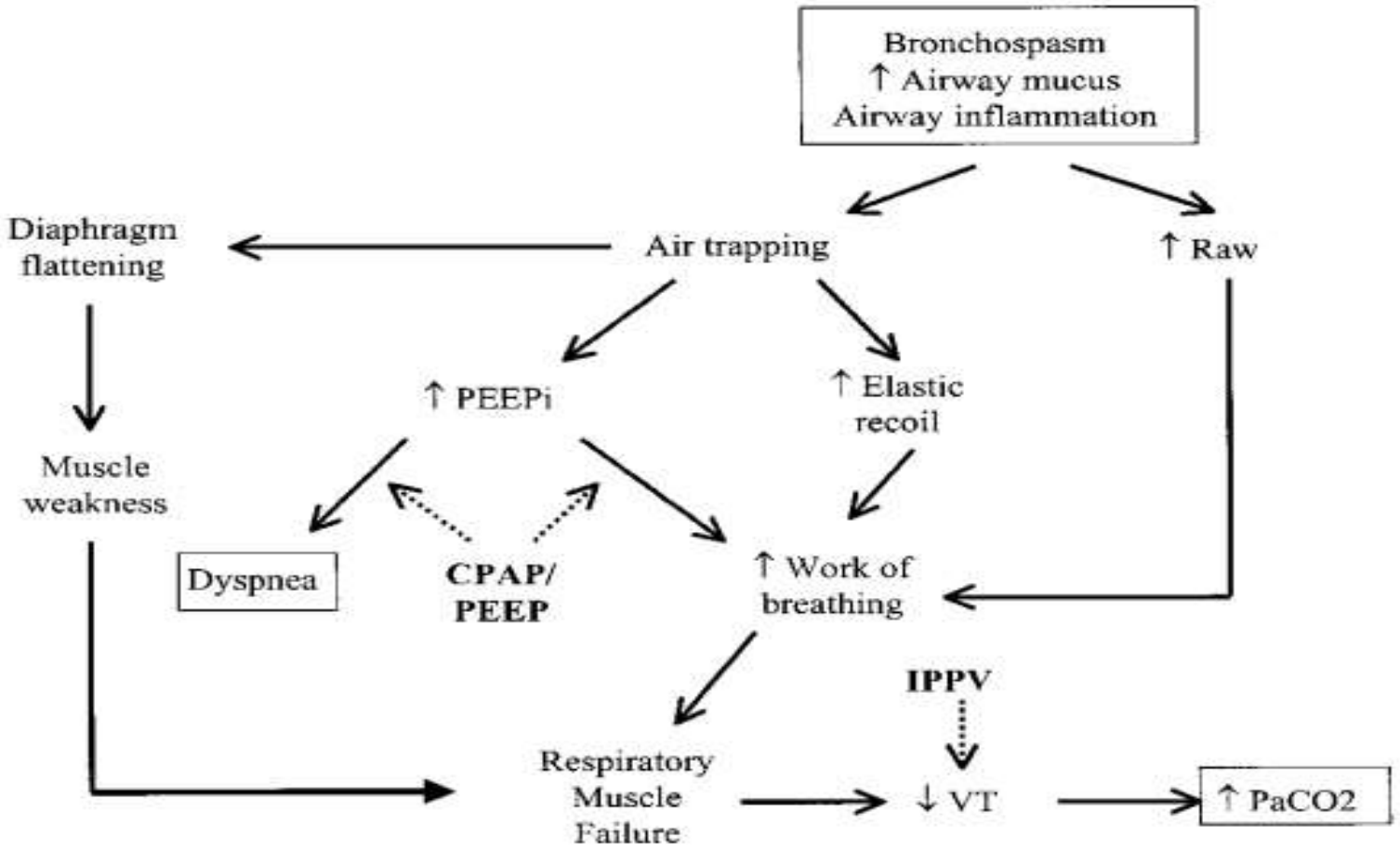
Definitions

- Respiratory failure:
  - type 1: $PaO_2 < 8$ kPa with normal or low PCO_2.
  - type 2: $PaO_2 < 8$ kPa with $PCO_2 > 6$kPa.

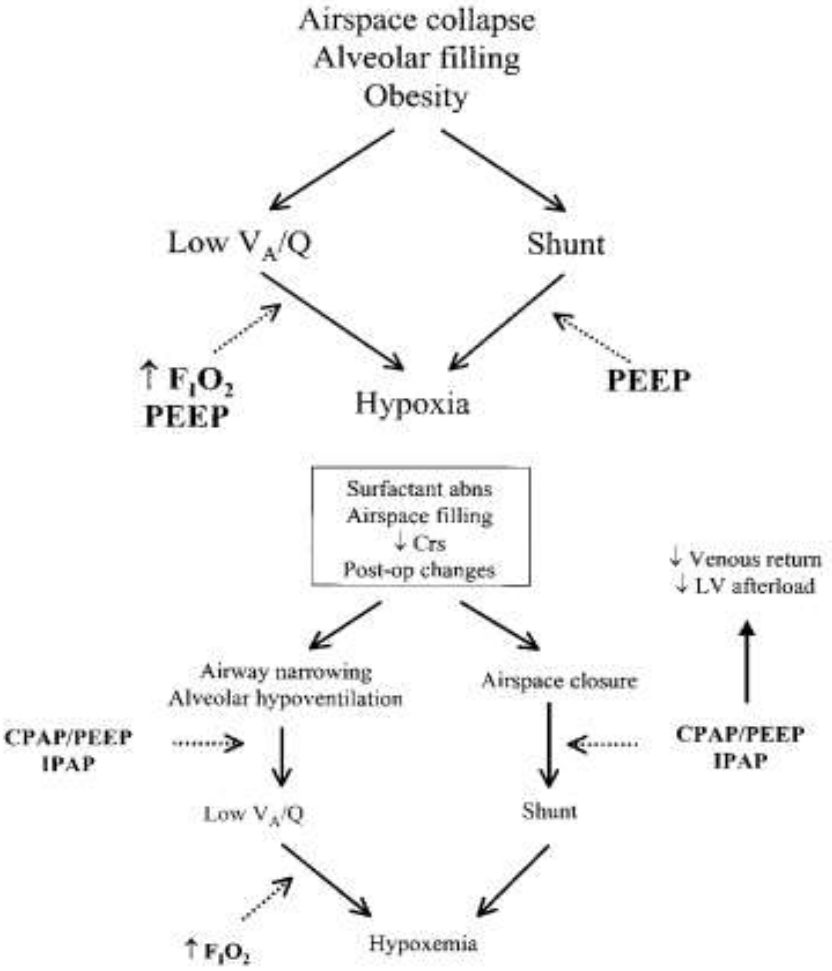
    - Acute hypercapnic : the patient will have no minor evidence of pre existing respiratory disease and arterial blood gas tension will show a high PCO_2, low pH and normal bicarbonate.
    - Chronic hypercapnic: evidence of chronic respiratory disease, high PCO_2, normal pH and high bicarbonate.
    - Acute on chronic: acute decompensation in an individual with significant pre exisiting hypercapnic respiratory failure , high PCO_2, low pH and high bicarbonate.

THORAX 2002.

Rationale for NIV in respiratory failure type 2



Type 1


Airspace collapse
Alveolar filling
Obesity
Low V_A/Q
Shunt
↑ F_IO_2
PEEP
Hypoxia
PEEP
Surfactant abns
Airspace filling
↓ Crs
Post-op changes
↓ Venous return
↓ LV afterload
Airway narrowing
Alveolar hypoventilation
Airspace closure
CPAP/PEEP
IPAP
CPAP/PEEP
IPAP
Low V_A/Q
Shunt
↑ F_IO_2
Hypoxemia

Decrease in nosocomial infection – German registry

- Pooled mean ventilator-associated pneumonia IDs were 1.58 and 5.44 cases per 1,000 ventilation days for NIV and IMV, respectively. The mean ID of pneumonia not associated with ventilation was lower with 0.58 cases per 1,000 patient days without ventilation
- the mean pneumonia ID in patients receiving IMV was four times higher than for patients receiving NIV, whereas data from this registry also show that NIV is associated with a threefold increase of the pneumonia ID in comparison to no ventilation, suggesting that ventilation is associated with a higher risk for pneumonia also in the absence of the endotracheal tube.

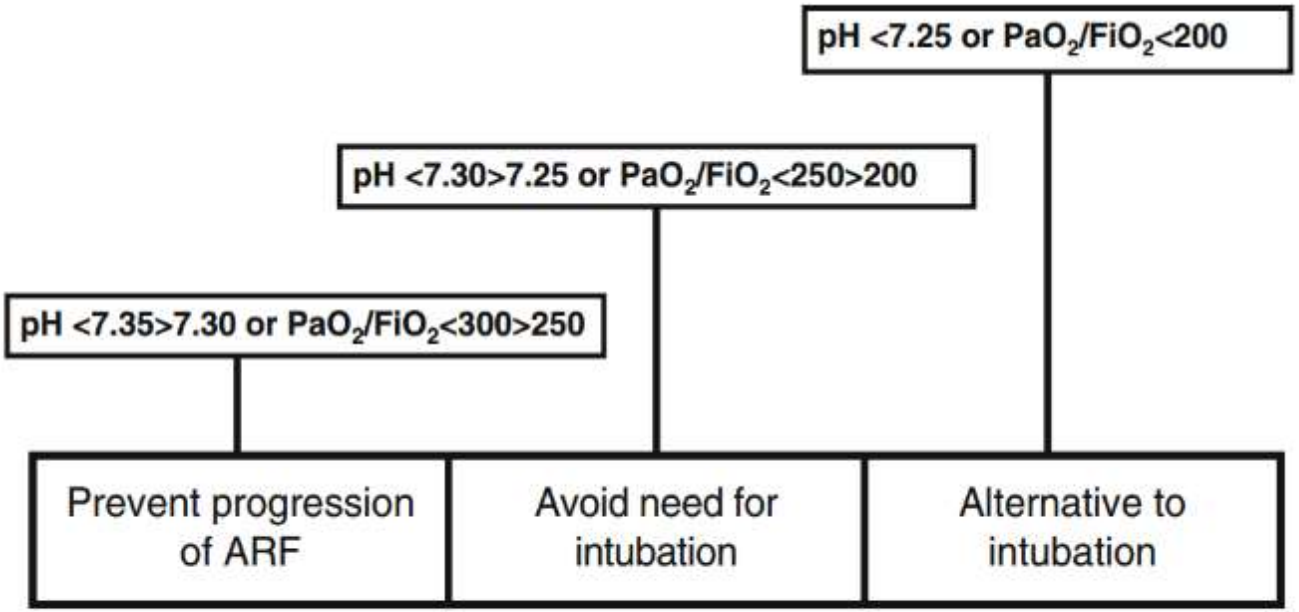
Intensive Care Med (2010) 36:971–978

Table 3 Characteristics of 6,869 pneumonia cases that occurred in 400 KISS-ICUs between 2005 and 2007

Parameter	Pneumonia not associated with ventilation	Pneumonia associated with NIV	Pneumonia associated with IMV	Total	*P* value[a]
No. of pneumonia cases	898	160	5,811	6,869	
Age of patients, years, mean (±SD), median (IQR)	67.8 (±15.2), 71 (60–78)	69.2 (±14.5), 70.5 (64–80)	64.2 (±15.9), 68 (56–76)	64.8 (±15.8), 68 (57–79)	<0.001
Sex of patients, male, no. (%)	635 (70.7)	109 (68.1)	3,903 (67.2)	4,647 (67.7)	0.106
Time from ICU admission to pneumonia, days, mean (±SD), median (IQR)	10.8 (±13.3), 7 (4–13)	11.5 (±10.0), 8 (5–14)	15.4 (±31.4), 10 (6–18)	14.7 (±29.4), 9 (5–17)	<0.001
Cases diagnosed >4 days of ICU-admission, no. (%)	656 (73.1)	122 (76.3)	4,912 (84.5)	5,690 (82.8)	<0.001
Secondary sepsis, no. (%)	30 (3.3)	10 (6.2)	356 (6.1)	396 (5.8)	0.004
Death, no. (%)	128 (13.3)	34 (21.3)	1,052 (18.1)	1,214 (17.7)	0.009
Cases with no pathogens isolated, no. (%)	439 (48.9)	73 (45.6)	1,250 (21.5)	1,762 (25.7)	<0.001
Cases with pathogens isolated, no. (%)	459 (51.1)	87 (54.4)	4,561 (78.5)	5,107 (74.3)	<0.001
Pathogens recovered from[b]					
ETA, no. (% of pneumonia cases)	362 (40.3)	60 (37.5)	3,953 (68.0)	4,375 (63.7)	<0.001
BAL/PSB, no. (% of pneumonia cases)	114 (12.7)	26 (16.3)	1,037 (17.8)	1,177 (17.1)	0.001
Blood culture, no. (% of pneumonia cases)	47 (5.2)	6 (3.8)	392 (6.7)	445 (6.5)	0.084

No number, *IMV* invasive mechanical ventilation, *NIV* noninvasive ventilation, *SD* standard deviation, *IQR* inter-quartile range, *ETA* endotracheal aspirate, *BAL* broncho-alveolar lavage, *PSB* protected specimen brush

Expectation from NIV



5.1 Timing of application

Optimism

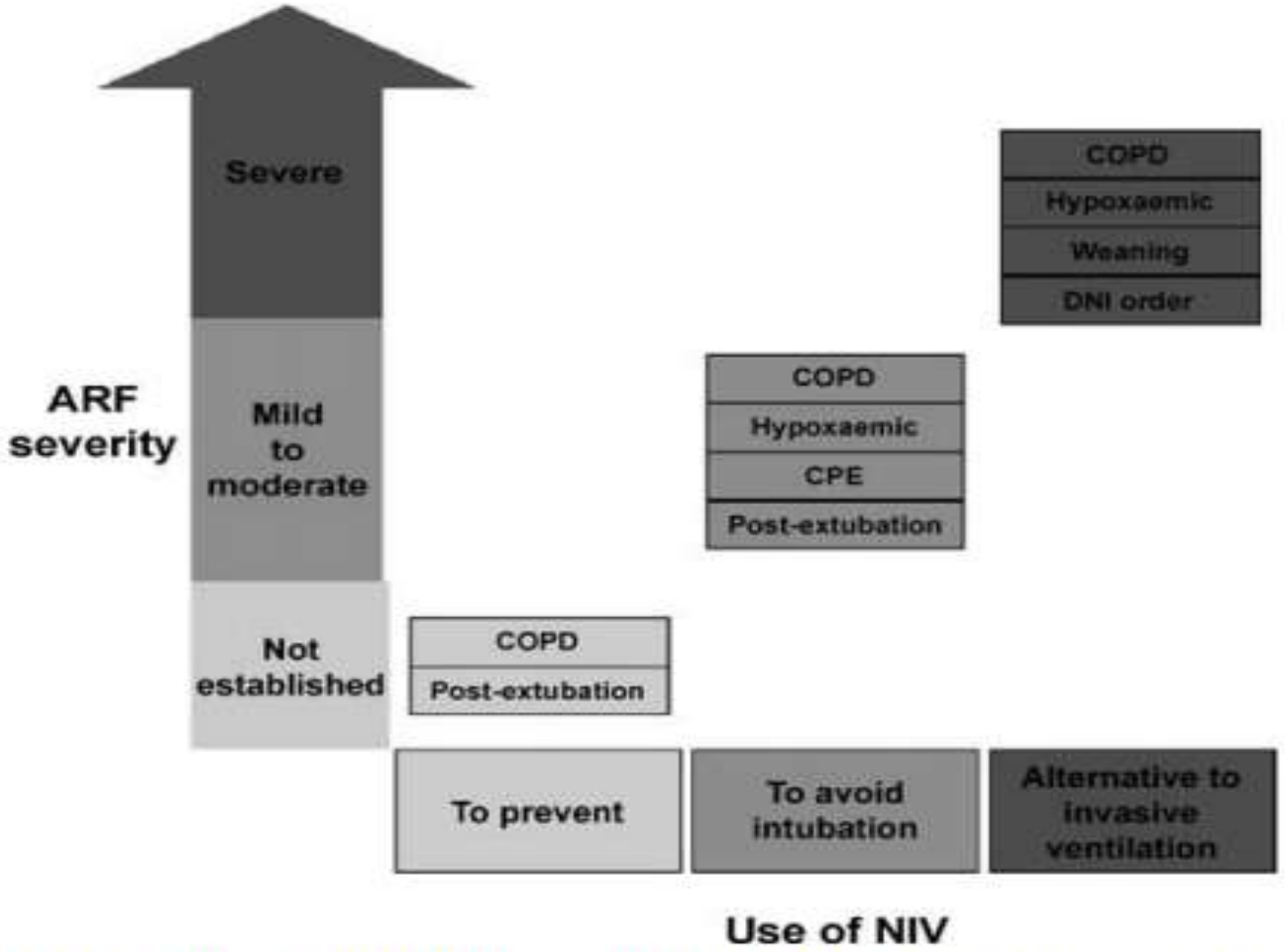


Fig. 1 Time of non-invasive ventilation (*NIV*) use with respect to severity of acute respiratory failure (*ARF*)

Vs not so optimistic

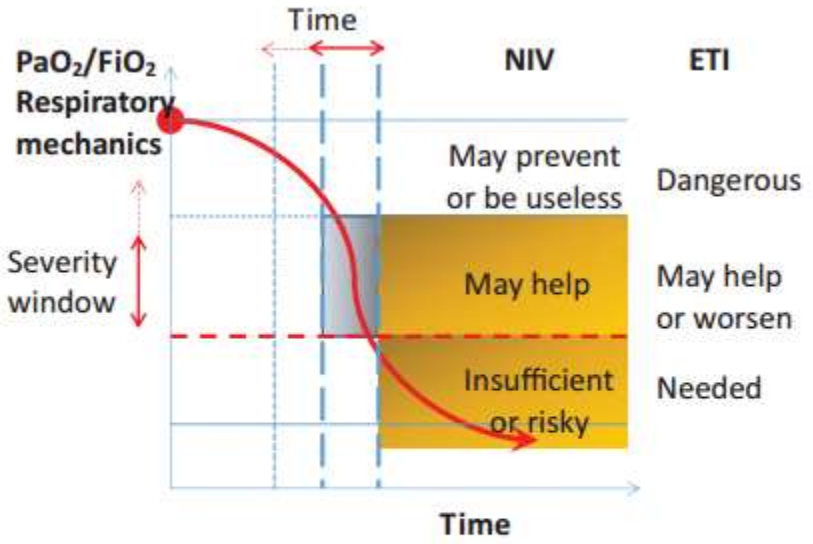


Fig. 1 Schematic representation of the time window and the severity window for the efficacy of noninvasive ventilation (NIV) compared with endotracheal intubation (ETI) in patients with acute respiratory failure.

Seminars in Respiratory and Critical Care Medicine Vol. 35 No. 4/2014

NIV in acute respiratory failure –level of evidence

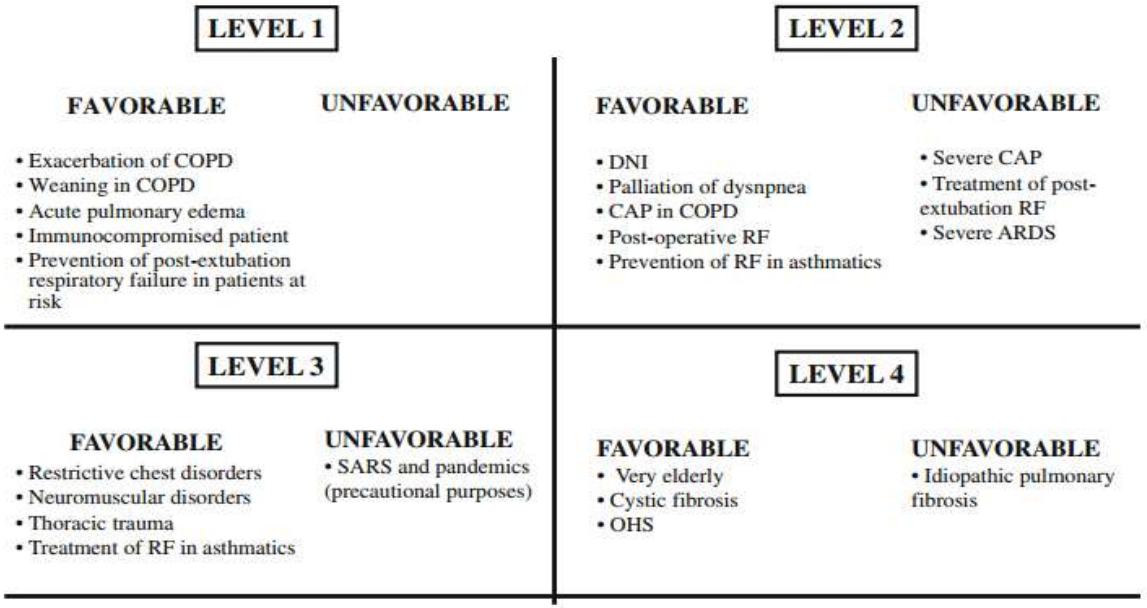


Fig. 11.1 Levels of scientific evidence: *LEVEL 1* systemic reviews based on randomized control trials with small confidence intervals; *LEVEL 2* reviews of single cohort studies, cohort studies or poorer quality randomized controlled trials; *LEVEL 3* reviews of case-controlled studies or individual case-controlled studies, *LEVEL 4* observational studies or case-controlled cohort studies of lesser quality

S. Nava and F. Fanfulla, *Non Invasive Artificial Ventilation*,
DOI: 10.1007/978-88-470-5526-1_11, © Springer-Verlag Italia 2014

Cardiogenic pulmonary edema

Rationale

Table 1. Potential Mechanisms of Action of CPAP and NIV in Patients With Acute Cardiogenic Pulmonary Edema

CPAP
Increased functional residual capacity
Reduced atelectasis
Reduced right-to-left intrapulmonary shunt
Reduced work of breathing from improved pulmonary compliance
Increased cardiac output from reduced pre-load and after-load
Reduced mitral regurgitation
NIV
Same benefits as CPAP
Unloads the respiratory muscles

CPAP = continuous positive airway pressure
NIV = noninvasive ventilation

- Recommendation –
  - ❑ CPAP has been shown to be effective in patients with cardiogenic pulmonary edema who remains hypoxic despite maximal medical therapy. NIV should be reserved for patients in whom CPAP is unsuccessful.

    Thorax 2002;57:192–211
  - ✓ CPAP/NIV should be used in patients with cardiogenic pulmonary edema with associated respiratory failure in absence of shock or acute coronary syndrome requiring urgent coronary revascularization.

    CMAJ, February 22, 2011, 183(3)
  - ➢ CPAP/NIV are equally effective in CPE; NIV is preferrable in patient with hypercapnic respiratory failure

    Indian J Crit Care Med April-June2006 Vol10 Issue2

Meta analysis 2006

Effect of non-invasive positive pressure ventilation (NIPPV) on mortality in patients with acute cardiogenic pulmonary oedema: a meta-analysis

John Victor Peter, John L Moran, Jennie Phillips-Hughes, Petra Graham, Andrew D Bersten

Lancet 2006; 367: 1155–63

Method

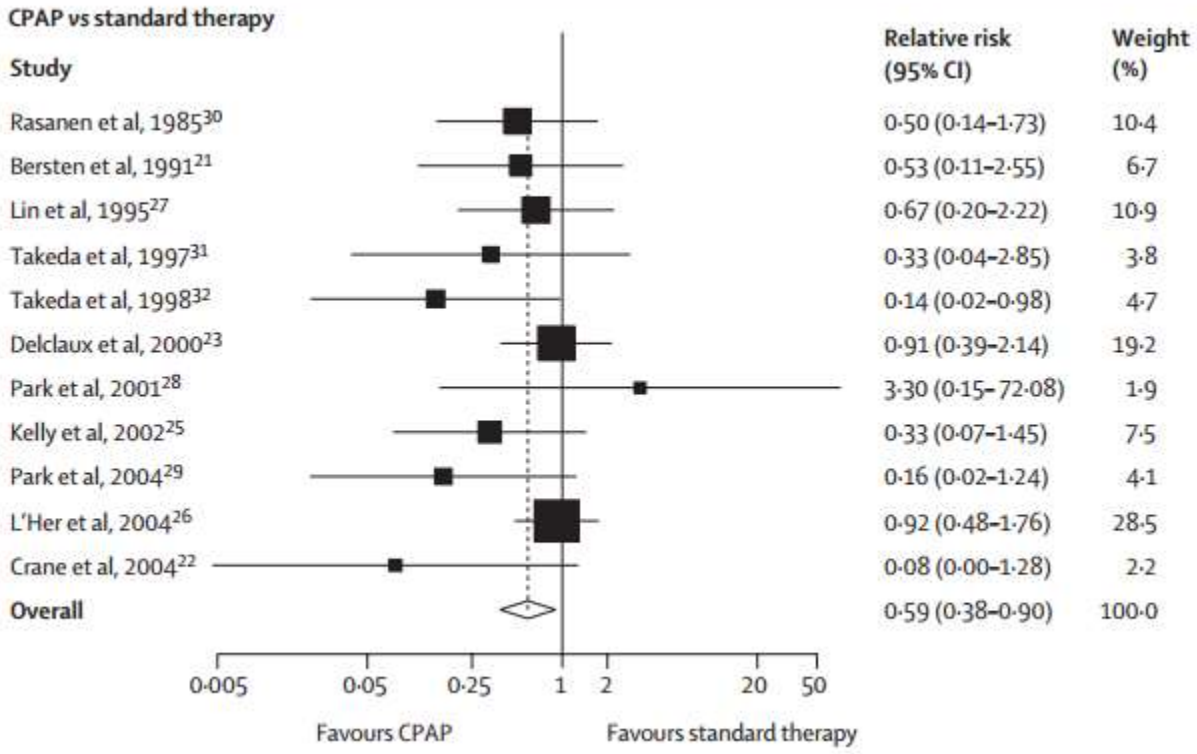
- Trial selection
  - Randomized trials on acute cardiogenic pulmonary oedema in human beings that compared CPAP or bilevel ventilation with standard therapy (oxygen by facemask, diuretics, nitrates, and other supportive care) or CPAP with bilevel ventilation were considered for inclusion.
  - Only trials reporting hospital mortality or the need for invasive mechanical ventilation were included.
- Outcome measures
  - Primary outcomes assessed were hospital mortality, defined as deceased when discharged from hospital, and the need for mechanical ventilation.
  - Secondary outcomes included failure rates of treatment (standard therapy or NIPPV), length of hospital stay (defined as the time from admission to discharge), duration of NIPPV, and incidence of new myocardial infarction.

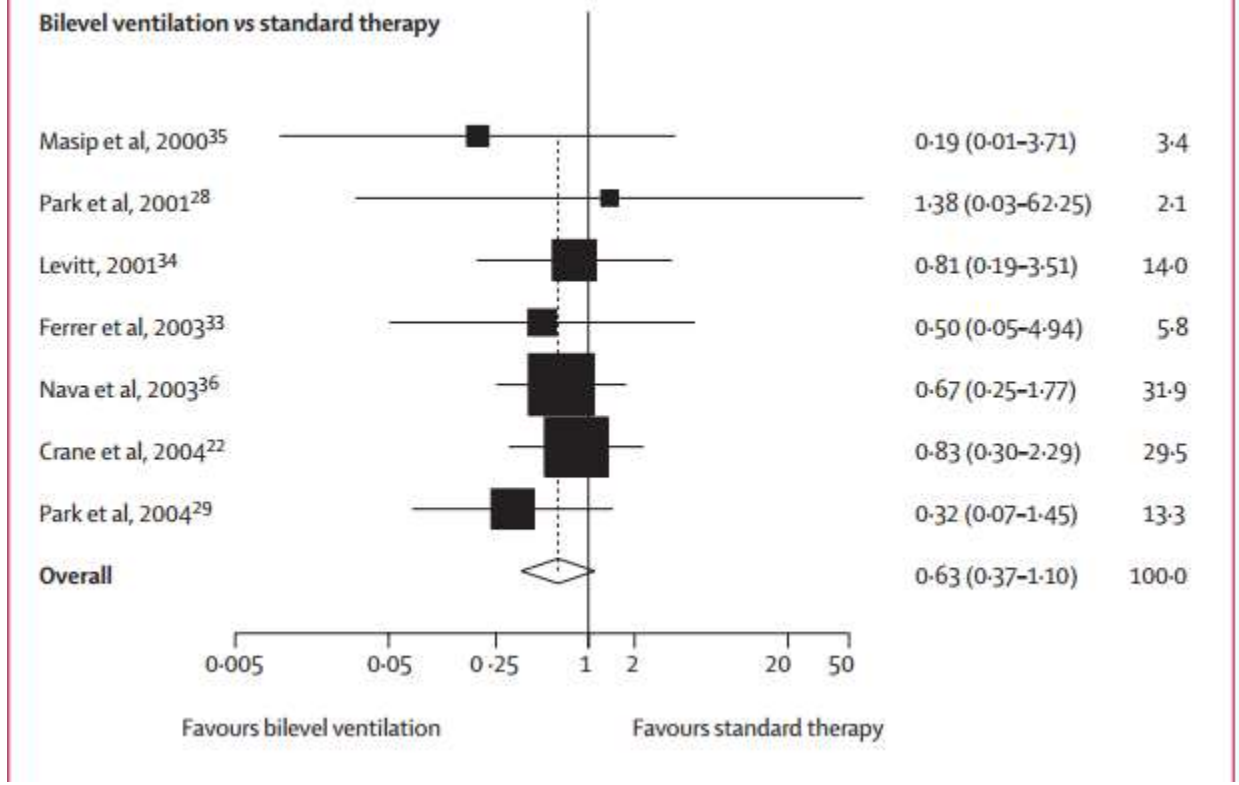
Main result

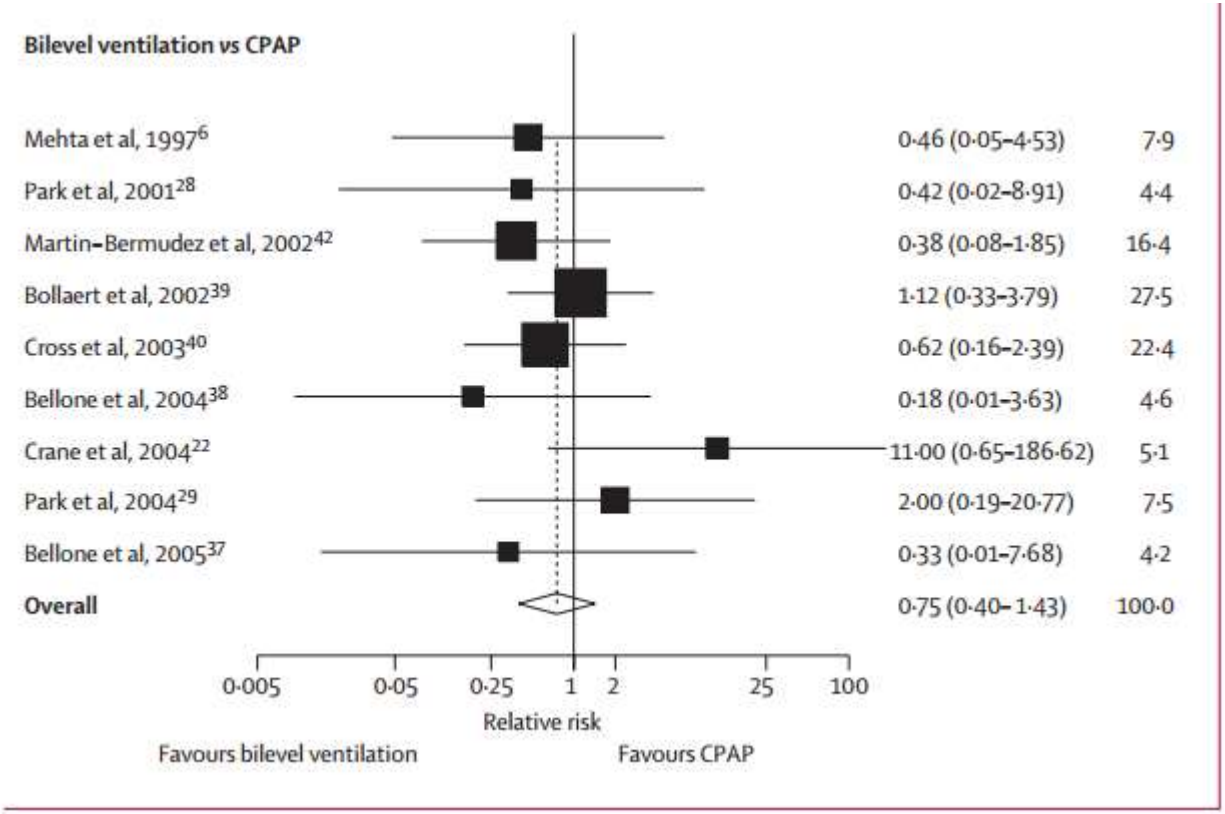
	Number of contributing studies	Total number of patients	Relative risk (95% CI)	p	I^2 (%)	Number needed to treat*	Number of events avoided per 1000 patients treated (95% CI)
Mortality							
CPAP vs standard therapy	11	263/269	0·59 (0·38–0·90)	0·015	11	10	101 (24–151)
Bilevel ventilation vs standard therapy	7	174/171	0·63 (0·37–1·10)	0·11	0	n/a	n/a
Bilevel ventilation vs CPAP	9	203/203	0·75 (0·40–1·43)	0·38	0	n/a	n/a
Need for mechanical ventilation							
CPAP vs standard therapy	12	288/295	0·44 (0·29–0·66)	0·0003	12	6	161 (98–204)
Bilevel ventilation vs standard therapy	7	174/171	0·50 (0·27–0·90)	0·02	21	7	136 (26–196)
Bilevel ventilation vs CPAP	9	175/178	0·94 (0·48–1·86)	0·86	0	n/a	n/a
Composite failure rates							
CPAP vs standard therapy	12	288/295	0·42 (0·27–0·65)	0·0005	37	5	220 (131–276)
Bilevel ventilation vs standard therapy	7	174/171	0·51 (0·30–0·87)	0·01	12	7	135 (36–193)
Bilevel ventilation vs CPAP	9	175/178	0·75 (0·44–1·30)	0·31	74	n/a	n/a
Author-defined failure rates							
CPAP vs standard therapy	6	187/179	0·45 (0·25–0·82)	0·009	40	5	198 (65–271)
Bilevel ventilation vs standard therapy	1	20/20	1·00 (0·07–14·9)	1·0	n/a	n/a	n/a
Bilevel ventilation vs CPAP	3	72/75	0·58 (0·21–1·56)	0·28	47	n/a	n/a
Incidence of new myocardial infarction							
CPAP vs standard therapy	3	74/77	0·83 (0·43–1·61)	0·58	0	n/a	n/a
Bilevel ventilation vs standard therapy	4	133/128	1·19 (0·68–2·10)	0·50	0	n/a	n/a
Bilevel ventilation vs CPAP	8	174/172	1·49 (0·92–2·42)	0·11	0	n/a	n/a

n/a=not calculated for non-significant results. *Number needed to treat for benefit.

Table 3: Effect of NIPPV on study outcomes


CPAP vs standard therapy
Study
Relative risk (95% CI)
Weight (%)
Rasanen et al, 1985[30]
0·50 (0·14–1·73)
10·4
Bersten et al, 1991[21]
0·53 (0·11–2·55)
6·7
Lin et al, 1995[27]
0·67 (0·20–2·22)
10·9
Takeda et al, 1997[31]
0·33 (0·04–2·85)
3·8
Takeda et al, 1998[32]
0·14 (0·02–0·98)
4·7
Delclaux et al, 2000[23]
0·91 (0·39–2·14)
19·2
Park et al, 2001[28]
3·30 (0·15–72·08)
1·9
Kelly et al, 2002[25]
0·33 (0·07–1·45)
7·5
Park et al, 2004[29]
0·16 (0·02–1·24)
4·1
L'Her et al, 2004[26]
0·92 (0·48–1·76)
28·5
Crane et al, 2004[22]
0·08 (0·00–1·28)
2·2
Overall
0·59 (0·38–0·90)
100·0
0·005
0·05
0·25
1
2
20
50
Favours CPAP
Favours standard therapy


Bilevel ventilation vs standard therapy
Masip et al, 2000[35]
Park et al, 2001[28]
Levitt, 2001[34]
Ferrer et al, 2003[33]
Nava et al, 2003[36]
Crane et al, 2004[22]
Park et al, 2004[29]
Overall
0·19 (0·01–3·71) 3·4
1·38 (0·03–62·25) 2·1
0·81 (0·19–3·51) 14·0
0·50 (0·05–4·94) 5·8
0·67 (0·25–1·77) 31·9
0·83 (0·30–2·29) 29·5
0·32 (0·07–1·45) 13·3
0·63 (0·37–1·10) 100·0
0·005
0·05
0·25
1
2
20
50
Favours bilevel ventilation
Favours standard therapy


Bilevel ventilation vs CPAP
Mehta et al, 1997[6]
Park et al, 2001[28]
Martin-Bermudez et al, 2002[42]
Bollaert et al, 2002[39]
Cross et al, 2003[40]
Bellone et al, 2004[38]
Crane et al, 2004[22]
Park et al, 2004[29]
Bellone et al, 2005[37]
Overall
0·46 (0·05–4·53) 7·9
0·42 (0·02–8·91) 4·4
0·38 (0·08–1·85) 16·4
1·12 (0·33–3·79) 27·5
0·62 (0·16–2·39) 22·4
0·18 (0·01–3·63) 4·6
11·00 (0·65–186·62) 5·1
2·00 (0·19–20·77) 7·5
0·33 (0·01–7·68) 4·2
0·75 (0·40–1·43) 100·0
0·005
0·05
0·25
1
2
25
100
Relative risk
Favours bilevel ventilation
Favours CPAP

Clinical trial –NIV vs CPAP (2011)

Method	Prospective multicenter RCT
Participants	200 patients presented with a clinical condition consistent with acute CPE were randomly assigned to receive NIV vs CPAP in emergency department of four tertiary care hospital. Patient with ongoing MI were excluded
Intervention	Bilevel positive pressure ventilation via face mask. According to protocol interventional treatment was given for 6hrs. Afterward patients were transferred to ICU if required intubation or to the ward if clinical condition did not improve.
Comparator	CPAP was given by Boussignac CPAP device.
Outcome	Primary outcome was combined event of hospital death or tracheal intubation. Secondary outcomes were resolution time, MI, length of hospital stay

Table 2 Primary outcomes

	NIPSV ($n = 99$)	CPAP ($n = 101$)	Difference (95% CI)	p
Death, n (%)	5 (5.0)	3 (2.9)	2.1% (−3.4 to 7.5)	0.563
Intubation, n (%)	10 (10.1)	7 (6.9)	3.2% (−4.9 to 11.5)	0.457
Combined events[a], n (%)	11 (11.1)	7 (6.9)	4.2% (−3.7 to 12.1)	0.485

Table 3 Outcomes in hypercapnic patients and in patients with high BNP (>500 pg/ml) in NIPSV and CPAP groups

	NIPSV	CPAP	Difference (95% CI)	p
Death, n/total (%)				
Hypercapnia	3/29 (10.3)	2/27 (7.4)	2.9% (−14.4 to 19.9)	0.997
High BNP	1/37 (2.7)	2/34 (5.9)	3.2% (−8.7 to 16.6)	0.603
Intubation n/total (%)				
Hypercapnia	7/29 (24.1)	4/27 (14.8)	9.3% (−11.9 to 29.4)	0.588
High BNP	7/37 (18.9)	4/34 (11.7)	2.2% (−10.4 to 24.0)	0.614
Combined events[a], n/total (%)				
Hypercapnia	8/29 (27.6)	5/27 (18.5)	9.1% (−12.7 to 30.9)	0.645
High BNP	7/37 (18.9)	4/34 (11.8)	7.1% (−9.5 to 23.7)	0.692

CPAP continuous positive airway pressure, *NIPSV* noninvasive pressure support ventilation, *BNP* brain natriuretic peptide

[a] When both events (death and intubation) occurred in the same patient, only the worst one (death) was considered

3CPO trial –NEJM July 2008

Method	The study was an open, randomized, controlled, parallel-group trial with three treatment groups: standard oxygen therapy, CPAP, and NIPPV.
participant	The inclusion criteria were an age of more than 16 years, a clinical diagnosis of acute cardiogenic pulmonary edema, pulmonary edema shown by a chest radiograph, a respiratory rate of more than 20 breaths per minute, and an arterial hydrogenion concentration of greater than 45 nmol per liter (pH <7.35). The exclusion criteria were a requirement for a lifesaving or emergency intervention, such as primary percutaneous coronary intervention; inability to give consent; or previous recruitment into the trial.
intervention	CPAP and NPPV were delivered through a full face mask by a resperionic synchrony ventilator. Supplementary oxygen was given at maximum rate of 15l/min with maximum FiO2 of .6 to maintain an O2 saturation >92%. All participants received their allocated treatment for at least 2hrs
outcome	Out of 1069 patients randomized 367 received standard oxygen therapy, 346 CPAP and 356 NIPPV. No difference was found in primary outcome i.e. 7 days mortality or in the composite outcome of 7 day mortality and intubation rate or in the secondary outcome i.e. 30 day mortality. There was significant benefit in patient rated dyspnea, Ph, HR, hypercapnia at 1 hours in NIV group (other secondary outcome)

Table 3. Primary and Secondary End Points for Patients Receiving Standard Oxygen Treatment and Those Receiving Noninvasive Ventilation (CPAP or NIPPV).*

Variable	Standard Oxygen Treatment (N=367)	CPAP or NIPPV (N=702)	Odds Ratio (95% CI)	P Value
Death within 7 days (% of patients)	9.8	9.5	0.97 (0.63 to 1.48)	0.87
Death within 30 days (% of patients)	16.4	15.2	0.92 (0.64 to 1.31)	0.64
Intubation within 7 days (% of patients)	2.8	2.9	1.05 (0.49 to 2.27)	0.90
Admission to critical care unit (% of patients)	40.5	45.2	1.21 (0.93 to 1.57)	0.15
Myocardial infarction (% of patients)				
WHO criteria	24.9	27.0	1.12 (0.84 to 1.49)	0.46
Universal criteria	50.5	51.9	1.06 (0.82 to 1.36)	0.66
			Difference between Means (95% CI)†	
Mean length of hospital stay (days)	10.5	11.4	0.9 (−0.2 to 2.0)	0.10
Mean change at 1 hr after start of treatment‡				
Dyspnea score§	3.9	4.6	0.7 (0.2 to 1.3)	0.008
Pulse rate (beats/min)	13	16	4 (1 to 6)	0.004
Blood pressure (mm Hg)				
Systolic	34	38	3 (−1 to 8)	0.17
Diastolic	22	22	0 (−3 to 3)	0.95
Respiratory rate (breaths/min)	7.1	7.2	0.2 (−0.8 to 1.1)	0.74
Peripheral oxygen saturation (%)	3.5	3.0	−0.4 (−1.4 to 0.6)	0.41
Arterial pH	0.08	0.11	0.03 (0.02 to 0.04)	<0.001
Arterial PaO_2 (kPa)	0.7	−0.6	−1.2 (−2.6 to 0.1)	0.07
Arterial $PaCO_2$ (kPa)	0.8	1.5	0.7 (0.4 to 0.9)	<0.001
Serum bicarbonate level (mmol/liter)	1.7	1.8	0.1 (−0.7 to 1.0)	0.77

Table 2. Treatment of Patients.*

Variable	Standard Oxygen Treatment (N=367)	CPAP (N=346)	NIPPV (N=356)	All Patients (N=1069)	P Value†
Initial treatment — % of patients					
Nitrates	93	88	91	90	0.11
Diuretics	90	89	89	89	0.89
Opioids	55	50	49	51	0.31
Inspired oxygen — liters/min	12±4	12±4	12±4	12±4	0.44
Ventilation pressure — cm of water	—	10±4	Inspiratory 14±5, expiratory 7±3	—	
Started assigned treatment — no./total no. (%)‡	365/366 (99.7)	337/343 (98.3)	344/354 (97.2)	1046/1063 (98.4)	0.02
Completed assigned treatment — no./total no. (%)§	298/363 (82.1)	285/340 (83.8)	267/352 (75.9)	850/1055 (80.6)	0.02
Changed to new treatment — no.					
Intubation	3	1	4		
CPAP	43	—	12		
NIPPV	13	5	—		
Standard treatment	—	31	49		
New treatment not stated	6	18	20		
Reason for not completing assigned treatment — no. (%)¶					
Patient discomfort	1 (0.3)	18 (5.2)	30 (8.4)		<0.001
Worsening arterial blood gas values	26 (7.1)	10 (2.9)	15 (4.2)		0.03
Respiratory distress	31 (8.4)	5 (1.4)	12 (3.4)		<0.001
Other	18 (4.9)	24 (6.9)	29 (8.1)		0.21

Meta analysis 2013

Non-invasive positive pressure ventilation (CPAP or bilevel NPPV) for cardiogenic pulmonary oedema (Review)

Vital FMR, Ladeira MT, Atallah ÁN

THE COCHRANE COLLABORATION®

This is a reprint of a Cochrane review, prepared and maintained by The Cochrane Collaboration and published in *The Cochrane Library* 2013, Issue 5

http://www.thecochranelibrary.com

- Main result
  - 32 studies (2916 participants), were included of generally low or uncertain risk of bias.
  - Compared with standard medical care, NPPV significantly reduced hospital mortality (RR 0.66, 95% CI 0.48 to 0.89) and endotracheal intubation (RR 0.52, 95% CI 0.36 to 0.75).
  - No difference in hospital length of stay with NPPV was found; however, intensive care unit stay was reduced by 1 day (WMD -0.89 days, 95% CI -1.33 to -0.45).
  - Compared with standard medical care ther was no significant increases in the incidence of acute myocardial infarction with NPPV during its application (RR 1.24, 95% CI 0.79 to 1.95) or after (RR 0.70, 95% CI 0.11 to 4.26).
  - Fewer adverse events with NPPV use (in particular progressive respiratory distress and neurological failure (coma)) were found when compared with standard medical care.

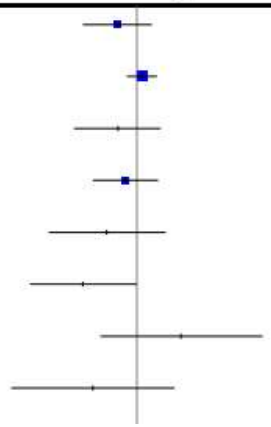
Analysis 1.1. Comparison 1 Hospital mortality, Outcome 1 NPPV (CPAP and BILEVEL) x SMC.

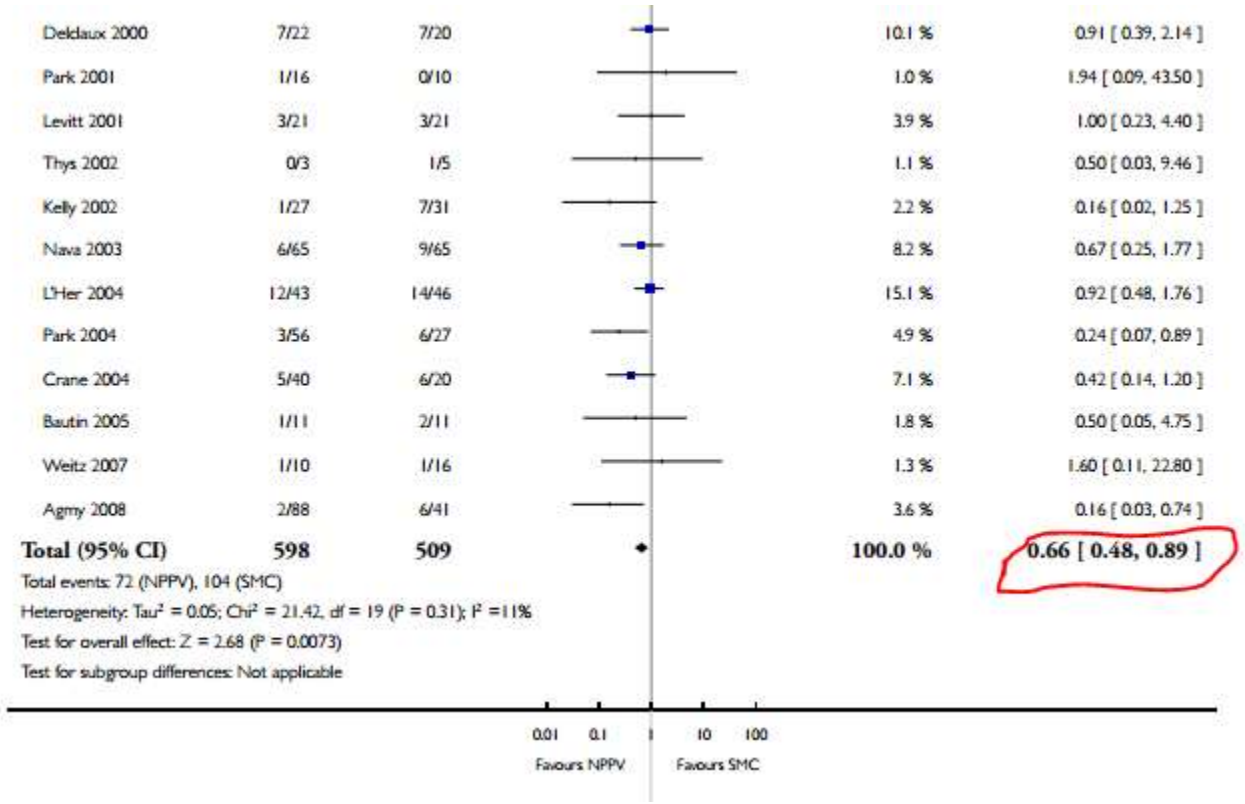
Review: Non-invasive positive pressure ventilation (CPAP or bilevel NPPV) for cardiogenic pulmonary oedema

Comparison: 1 Hospital mortality

Outcome: 1 NPPV (CPAP and BILEVEL) x SMC

Study or subgroup	NPPV n/N	SMC n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
Räsänen 1985	3/20	6/20		5.4 %	0.50 [0.14, 1.73]
Lin 1991	17/40	14/40		18.5 %	1.21 [0.70, 2.12]
Bersten 1991	2/20	4/20		3.5 %	0.50 [0.10, 2.43]
Lin 1995	4/50	6/50		5.7 %	0.67 [0.20, 2.22]
Takeda 1997	1/15	3/15		2.0 %	0.33 [0.04, 2.85]
Takeda 1998	1/11	7/11		2.4 %	0.14 [0.02, 0.98]
Sharon 2000	2/20	0/20		1.0 %	5.00 [0.26, 98.00]
Masip 2000	0/20	2/20		1.0 %	0.20 [0.01, 3.92]




Deklaux 2000 7/22 7/20 10.1 % 0.91 [0.39, 2.14]
Park 2001 1/16 0/10 1.0 % 1.94 [0.09, 43.50]
Levitt 2001 3/21 3/21 3.9 % 1.00 [0.23, 4.40]
Thys 2002 0/3 1/5 1.1 % 0.50 [0.03, 9.46]
Kelly 2002 1/27 7/31 2.2 % 0.16 [0.02, 1.25]
Nava 2003 6/65 9/65 8.2 % 0.67 [0.25, 1.77]
L'Her 2004 12/43 14/46 15.1 % 0.92 [0.48, 1.76]
Park 2004 3/56 6/27 4.9 % 0.24 [0.07, 0.89]
Crane 2004 5/40 6/20 7.1 % 0.42 [0.14, 1.20]
Bautin 2005 1/11 2/11 1.8 % 0.50 [0.05, 4.75]
Weitz 2007 1/10 1/16 1.3 % 1.60 [0.11, 22.80]
Agmy 2008 2/88 6/41 3.6 % 0.16 [0.03, 0.74]
Total (95% CI) 598 509 100.0 % 0.66 [0.48, 0.89]
Total events: 72 (NPPV), 104 (SMC)
Heterogeneity: Tau² = 0.05; Chi² = 21.42, df = 19 (P = 0.31); I² =11%
Test for overall effect: Z = 2.68 (P = 0.0073)
Test for subgroup differences: Not applicable
0.01 0.1 1 10 100
Favours NPPV
Favours SMC

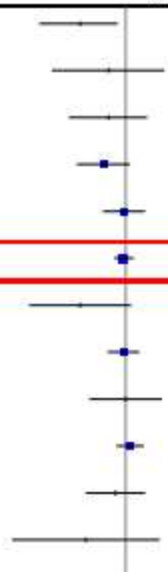
Analysis 15.1. Comparison 15 Hospital or 7-day mortality, Outcome 1 NPPV (CPAP and BILEVEL) X SMC.

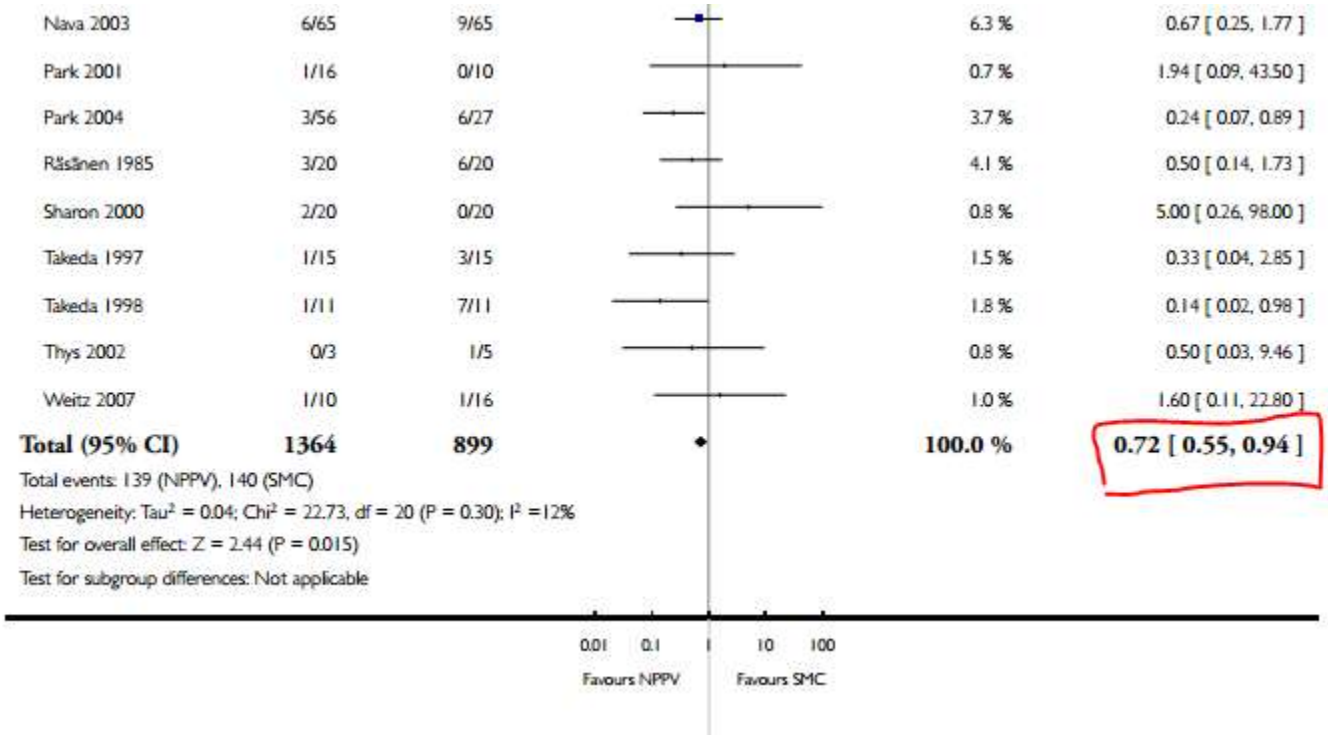
Review: Non-invasive positive pressure ventilation (CPAP or bilevel NPPV) for cardiogenic pulmonary oedema

Comparison: 15 Hospital or 7-day mortality

Outcome: 1 NPPV (CPAP and BILEVEL) X SMC

Study or subgroup	NPPV n/N	SMC n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
Agmy 2008	2/88	6/41		2.7 %	0.16 [0.03, 0.74]
Bautin 2005	1/11	2/11		1.3 %	0.50 [0.05, 4.75]
Bersten 1991	2/20	4/20		2.6 %	0.50 [0.10, 2.43]
Crane 2004	5/40	6/20		5.5 %	0.42 [0.14, 1.20]
Delclaux 2000	7/22	7/20		7.9 %	0.91 [0.39, 2.14]
Gray 2008	67/766	36/390		22.6 %	0.95 [0.64, 1.39]
Kelly 2002	1/27	7/31		1.6 %	0.16 [0.02, 1.25]
L'Her 2004	12/43	14/46		12.0 %	0.92 [0.48, 1.76]
Levitt 2001	3/21	3/21		3.0 %	1.00 [0.23, 4.40]
Lin 1991	17/40	14/40		14.9 %	1.21 [0.70, 2.12]
Lin 1995	4/50	6/50		4.4 %	0.67 [0.20, 2.22]
Masip 2000	0/20	2/20		0.8 %	0.20 [0.01, 3.92]




Nava 2003 6/65 9/65 6.3 % 0.67 [0.25, 1.77]
Park 2001 1/16 0/10 0.7 % 1.94 [0.09, 43.50]
Park 2004 3/56 6/27 3.7 % 0.24 [0.07, 0.89]
Räsänen 1985 3/20 6/20 4.1 % 0.50 [0.14, 1.73]
Sharon 2000 2/20 0/20 0.8 % 5.00 [0.26, 98.00]
Takeda 1997 1/15 3/15 1.5 % 0.33 [0.04, 2.85]
Takeda 1998 1/11 7/11 1.8 % 0.14 [0.02, 0.98]
Thys 2002 0/3 1/5 0.8 % 0.50 [0.03, 9.46]
Weitz 2007 1/10 1/16 1.0 % 1.60 [0.11, 22.80]
Total (95% CI) 1364 899 100.0 % 0.72 [0.55, 0.94]
Total events: 139 (NPPV), 140 (SMC)
Heterogeneity: Tau² = 0.04; Chi² = 22.73, df = 20 (P = 0.30); I² =12%
Test for overall effect: Z = 2.44 (P = 0.015)
Test for subgroup differences: Not applicable
0.01 0.1 1 10 100
Favours NPPV
Favours SMC

- Conclusion
  - NIV should be the respiratory support of choice in cardiogenic pulmonary edema presented with respiratory failure.
  - CPAP should be chosen over bilevel NPPV i/v/o more robust evidence favoring the former.

Pneumonia

- Recommendation
  - CPAP improves oxygenation in patients with diffuse pneumonia who remain hypoxic despite maximum medical treatment. NIV can be used as an alternative to tracheal intubation if the patient becomes hypercapnic. [C] In this context, patients who would be candidates for intubation if NIV fails should only received NIV in an ICU. [D]

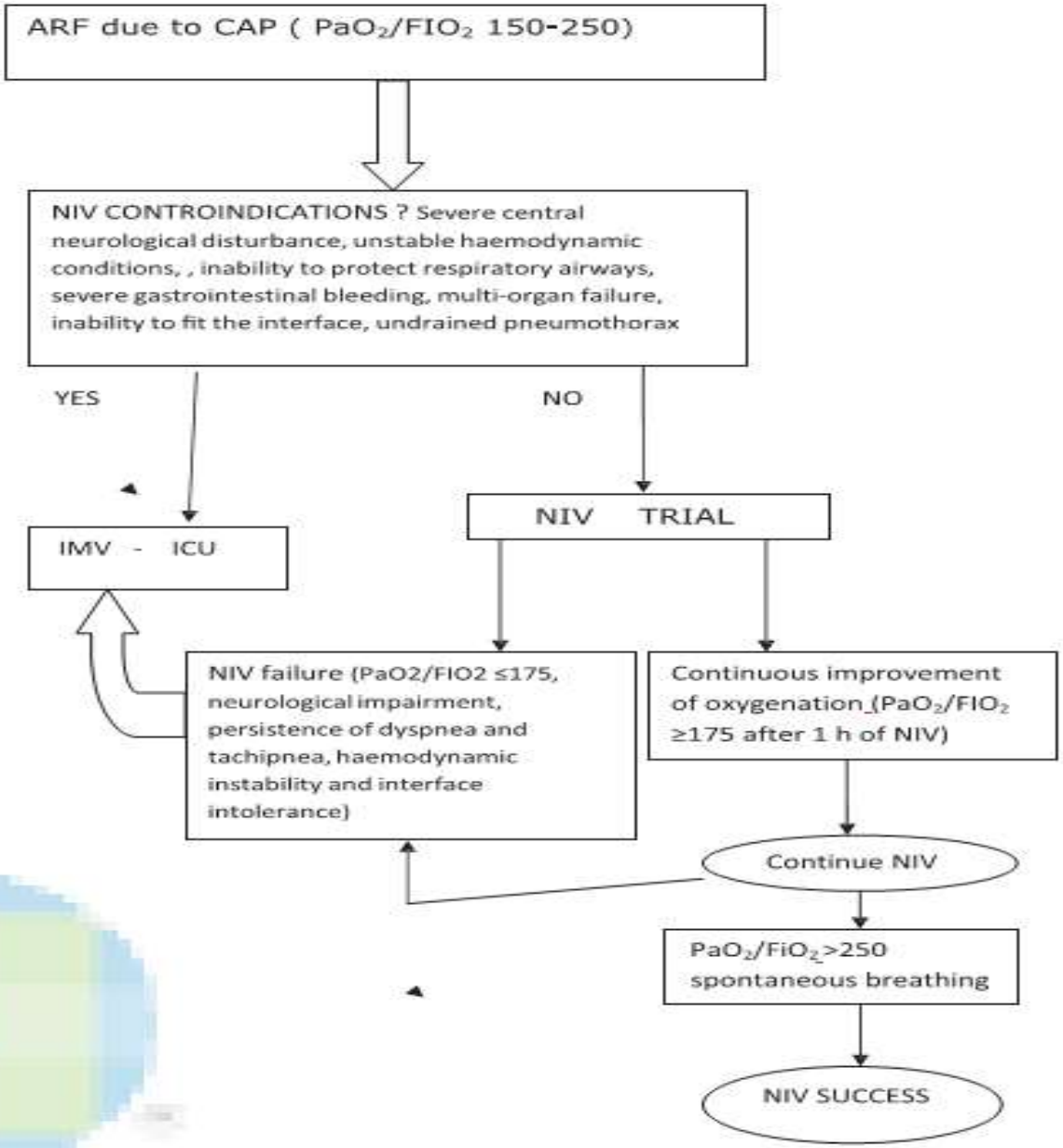
    Thorax 2002
  - no recommendation could be made for NIV/CPAP in severe CAP without COPD.

    CMAJ 2011

Table 2. Variables associated with failure of non-invasive ventilation

	NIV success 95 (74.9%) Mean ± SD	NIV failure 32 (25.1%) Mean ± SD	*P* value
Age	61 ± 21	63 ± 15	
Male	59 (62.1%)	17 (53.1%)	
Female	36 (37.9%)	15 (46.9%)	
SAPS II	26 ± 13	32 ± 10	0.01
CURB 65	2 ± 1	2 ± 1	0.12
Kelly scale	1 ± 1	1 ± 1	0.11
Co-morbidities	51	20	0.03
Lobes (n°)	3 ± 1	3 ± 1	0.14
Chest X-ray score*	7 ± 2	10 ± 3	0.003
Chest X-ray worsening	9	24	0.01
RMU stay (h.)	133 ± 124	146 ± 149	0.16
NIV duration (h.)	104 ± 108	127 ± 135	0.07
C-R Prot	21 ± 8	27 ± 10	0.10
LDH	423 ± 412	791 ± 306	0.003
Respiratory rate at admission	32 ± 6	33 ± 4	0.11
Heart rate at admission	104 ± 13	104 ± 11	0.12
$PaCO_2$ at admission	54 ± 39	52 ± 23	0.08
pH at admission	7.35 ± 0.02	7.35 ± 0.01	0.16
PaO_2/FiO_2 at admission	169 ± 45	140 ± 42	0.006
A-aDO_2 at admission	108 ± 81	174 ± 23	0.001
Respiratory rate after 1 h	26 ± 4	31 ± 5	0.03
Heart rate after 1 h	94 ± 9	106 ± 12	0.04
$PaCO_2$ after 1 h	48 ± 24	46 ± 17	0.11
pH after 1 h	7.37 ± 0.01	7.35 ± 0.02	0.13
PaO_2/FiO_2 after 1 h	211 ± 45	174 ± 84	0.001
A-aDO_2 after 1 h	129 ± 62	165 ± 125	0.001

*Opravil chest X-ray score.


ARF due to CAP (PaO2/FIO2 150-250)
NIV CONTROINDICATIONS ? Severe central neurological disturbance, unstable haemodynamic conditions, , inability to protect respiratory airways, severe gastrointestinal bleeding, multi-organ failure, inability to fit the interface, undrained pneumothorax
YES
NO
IMV - ICU
NIV TRIAL
NIV failure (PaO2/FIO2 ≤175, neurological impairment, persistence of dyspnea and tachipnea, haemodynamic instability and interface intolerance)
Continuous improvement of oxygenation (PaO2/FIO2 ≥175 after 1 h of NIV)
Continue NIV
PaO2/FiO2>250 spontaneous breathing
NIV SUCCESS

NIV in ARDS –physiology (beneficial)

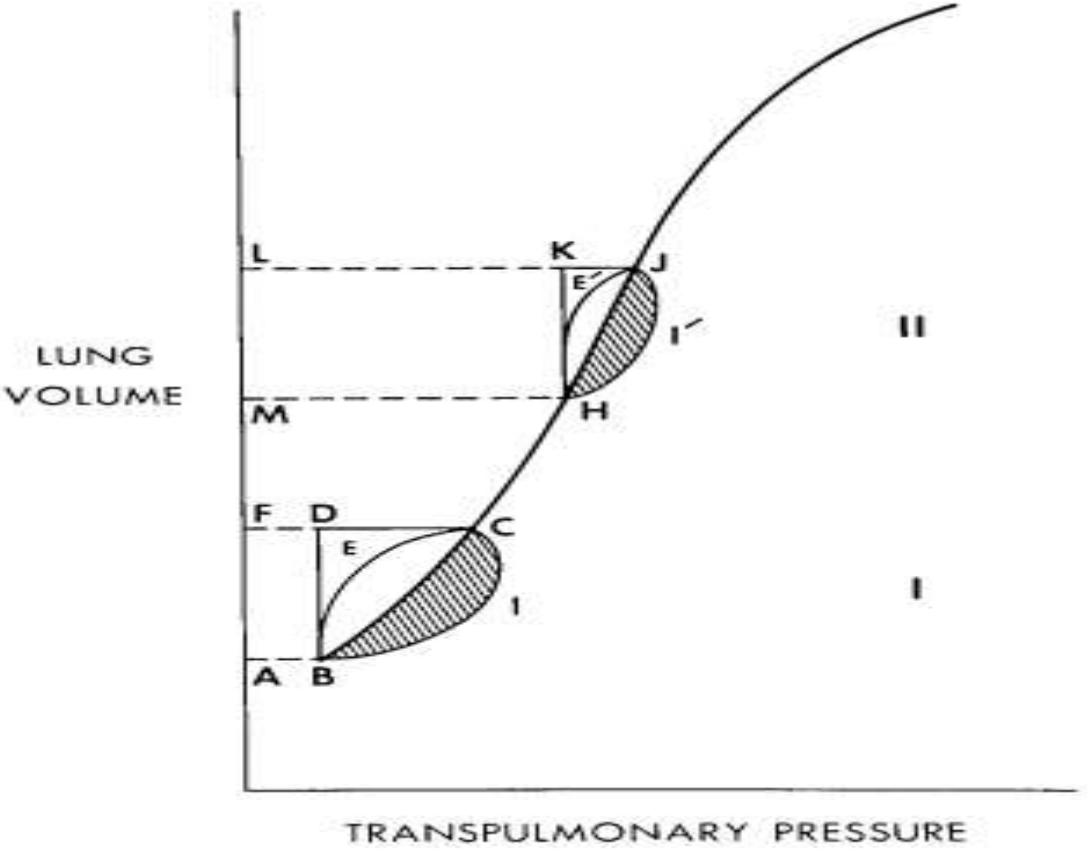
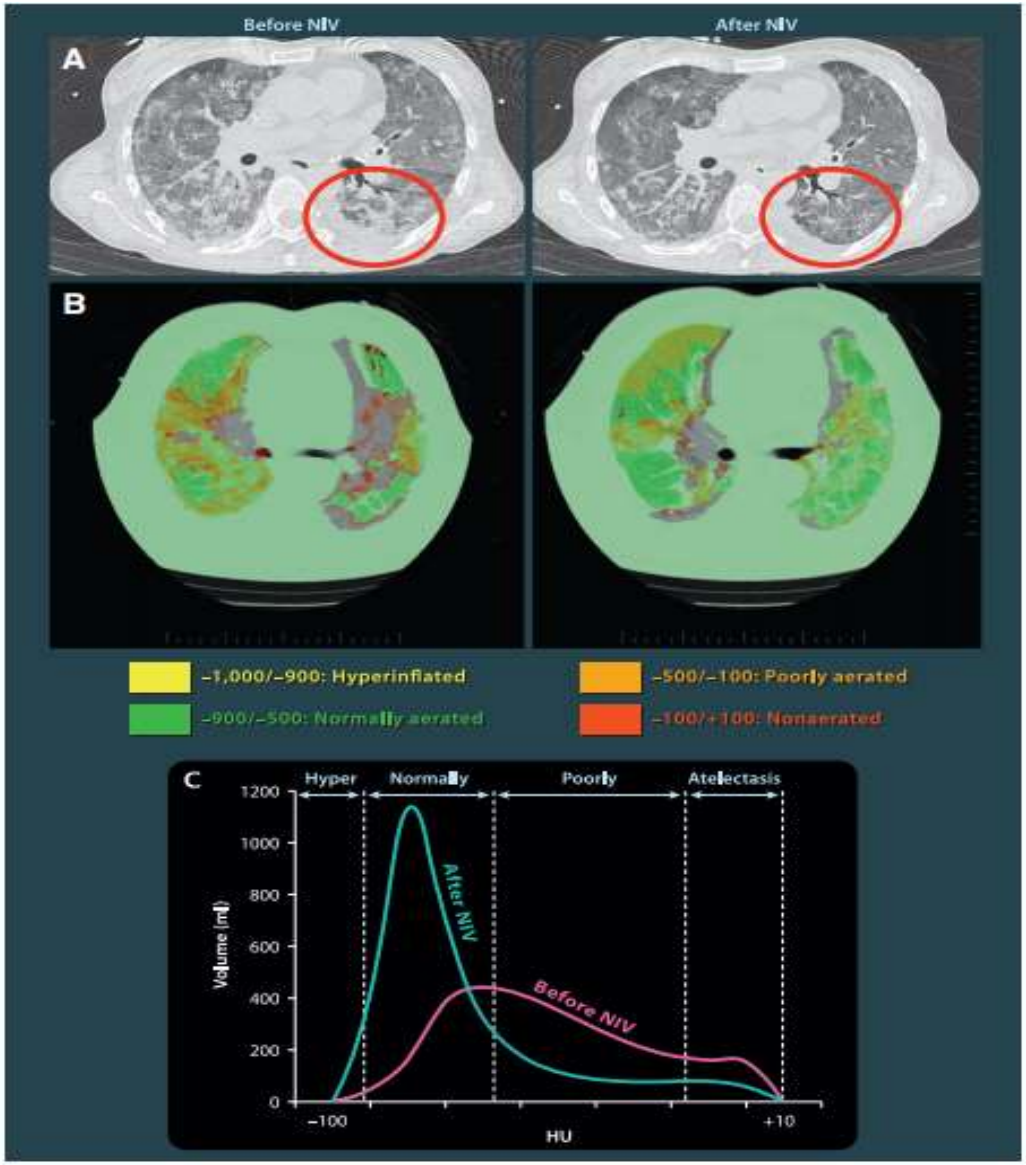


FIG. 2. Pressure–volume diagram of elastic and resistive (nonelastic) work done on the lungs. I. Breathing at ambient airway pressures (via T-tube). II. Breathing with CPAP. Solid line BCHJ is the elastic pressure–volume curve for the lung, determined by measuring transpulmonary pressures at the instant of zero flow. Hatched areas represent nonelastic work (BIC and HI'J). Measured elastic work is represented by BCD and HJK. A component of elastic work done on the lung is not considered. In the absence of CPAP, this component is normally small (ABDF), and about half of the work is done by the inspiratory muscles and half by elastic recoil of the chest wall. These contributions both diminish with CPAP, so that most or all of MHKL represents work done by the CPAP system.


Before NIV
After NIV
A
B
–1,000/–900: Hyperinflated
–900/–500: Normally aerated
–500/–100: Poorly aerated
–100/+100: Nonaerated
C
Hyper
Normally
Poorly
Atelectasis
1200
1000
800
600
400
200
0
Volume (ml)
After NIV
Before NIV
–100
+10
HU

or harmful

Method	Prospective observational study
Participants	Consecutive patients receiving NIV for acute hypoxemic respiratory failure
Intervention	NIV was given according to an uniform algorithm targeting tidal volume of 6-8 ml/kg of predicted body weight. The lowest pressure support level allowed was 7cm of H2O.
Measurement	Expired tidal volume was averaged and respiratory and hemodynamic variables were systematically recorded at each noninvasive ventilation session
Result	62 patient were recruited. The median (interquartile range) expired tidal volume averaged over all noninvasive ventilation sessions (mean expired tidal volume) was 9.8mL/kg predicted body weight (8.1–11.1mL/kg predicted body weight). The mean expired tidal volume was significantly higher in patients who failed noninvasive ventilation as compared with those who succeeded (10.6mL/kg predicted body weight [9.6–12.0] vs 8.5mL/kg predicted body weight [7.6–10.2]; $p = 0.001$).

Hypoxemic Respiratory Failure at Noninvasive Ventilation Initiation

Demographic and Clinical Data	NIV Success ($n = 30$)	NIV Failure ($n = 32$)	p
Age, yr	58 (39–67)	65 (58–77)	0.06
Male gender, n (%)	18 (60.0)	22 (68.7)	0.60
Simplified Acute Physiology Score II at admission (30)	30 (22–38)	41 (35–51)	<0.001
SOFA at NIV start	4 (3–7)	6 (5–8)	0.01
Respiratory SOFA	3 (2–3)	3 (2–4)	0.05
Coagulation SOFA	0 (0–1)	0 (0–2)	0.26
Liver SOFA	0 (0–1)	0 (0–1)	0.81
Cardiovascular SOFA	0 (0–0)	0 (0–2)	0.09
CNS SOFA	0 (0–0)	0 (0–1)	0.02
Renal SOFA	0 (0–1)	1 (0–2)	0.21
Immunosuppression	2 (6.7)	12 (37.5)	0.005
Arterial blood gases before NIV			
pH	7.41 (7.38–7.45)	7.45 (7.38–7.48)	0.09
Pao_2, mm Hg	70 (58–92)	69 (53–81)	0.14
Fio_2	0.5 (0.3–0.7)	0.6 (0.4–0.7)	0.45
Pao_2/Fio_2, mm Hg	177 (133–219)	122 (98–191)	0.02
$Paco_2$, mm Hg	36 (32–42)	32 (29–40)	0.15
Co_2t, mmol/L	25 (20–26)	23 (20–26)	0.50
Lactates, mmol/L	1.4 (0.9–2.9)	1.7 (1.3–2.6)	0.30
Increase in Pao_2/Fio_2 ratio after 1 hr of NIV	44 (−67 to 91)	41 (6–104)	0.43
Pao_2/Fio_2 categorization, n (%)*			1.00
Mild hypoxemia	14 (47)	15 (47)	
Moderate-to-severe hypoxemia	16 (53)	17 (53)	
Bilateral infiltrates on chest radiograph, n (%)	22 (73)	25 (78)	0.77

TABLE 3. Multivariate Analysis of Risk Factors for Noninvasive Ventilation Failure in Patients With De Novo Acute Hypoxemic Respiratory Failure

Risk Factors	Unadjusted Hazard Ratio (95% CI)	p	Adjusted Hazard Ratio (95% CI)[a]	p
Simplified Acute Physiology Score II (30)	1.026 (1.008–1.043)	0.011	1.024 (1.007–1.041)	0.013
Immunosuppression	2.207 (1.054–4.622)	0.045	1.351 (0.598–3.056)	0.476
Pao_2/Fio_2 before NIV	0.995 (0.990–1.001)	0.114	0.995 (0.989–1.001)	0.109
Mean expired tidal volume during NIV, per mL/kg predicted body weight	1.318 (1.109–1.567)	0.002	1.286 (1.069–1.547)	0.008

NIV = noninvasive ventilation.

[a]Adjusted hazard ratio obtained by Cox regression.

Recommendation

- In this context, patients who would be considered for intubation if NIV fails should only receive NIV in an ICU. [**D**]

  Thorax 2002;57:192–211

- We make no recommendation about the use of noninvasive positive-pressure ventilation in patients who have acute lung injury, because of a lack of RCTs.
- We recommend that continuous positive airway pressure not be used in patients who have acute lung injury (grade 1C recommendation)

  CMAJ, February 22, 2011, 183(3)

Clinical trials –NIV vs MV (NEJM 1998)

Method	Prospective RCT
Participant	Inclusion criteria : Acute respiratory distress, RR>35, P/F<200 Exclusion criteria: COPD, CPE, MOF, encephalopathy, shock, etc
intervention	Patients were randomly assigned to receive NIV or IMV. NIV was given through full face mask. IPAP was set to achieve a tidal volume of 8-10ml/kg and RR <25; whereas EPAP was set to achieve FiO2 <.6
Comparator	In conventional ventilation group patient receive ACMV with TV 10ml/kg, PEEP titrated to achieve FiO2 <.6 and 14-18 breth/min
Outcome	Primary outcome – gas exchange and complication of MV Secondary outcome – Mortality, ventilator days and ICU stay.

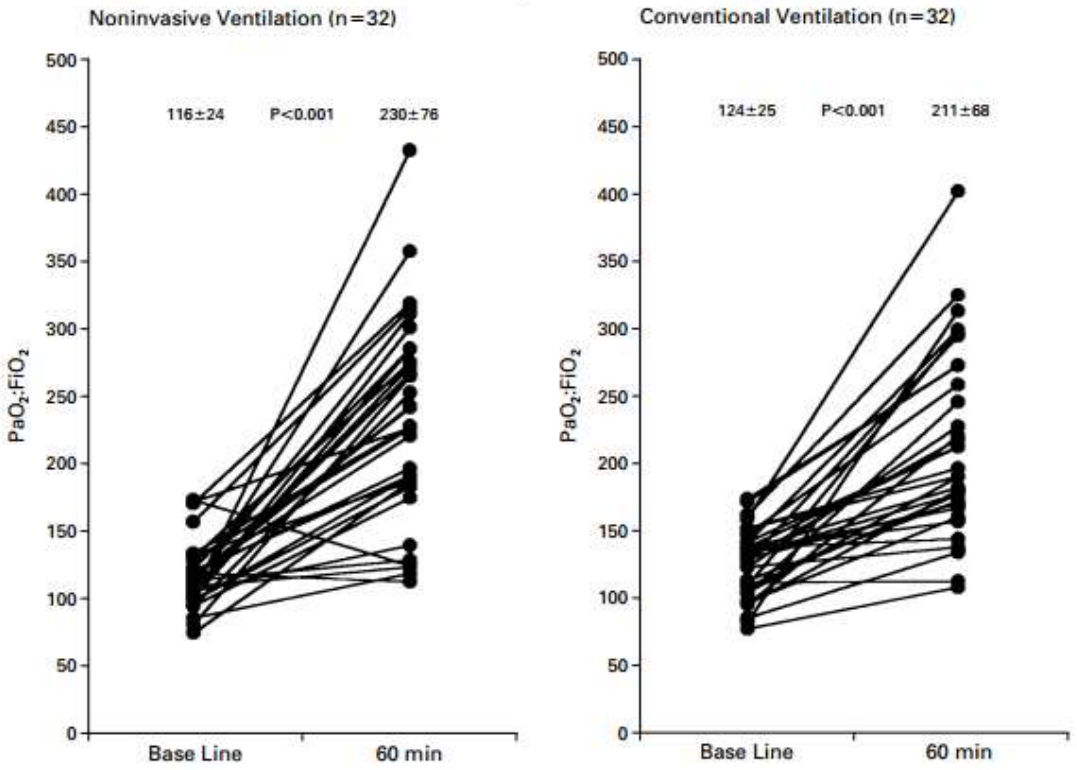


Figure 1. The Ratio of the Partial Pressure of Arterial Oxygen to the Fraction of Inspired Oxygen (PaO_2:FiO_2) at Base Line and after One Hour of Mechanical Ventilation in Patients with Acute Respiratory Failure in the Noninvasive-Ventilation and Conventional-Ventilation Groups.

A paired t-test was used for the statistical comparison. The degree of improvement in gas exchange after the start of mechanical ventilation was similar in the two groups. The values shown within the panels are means ±SD.

TABLE 2. SERIOUS COMPLICATIONS AND COMPLICATIONS RESULTING IN DEATH.

VARIABLE*	NONINVASIVE-VENTILATION GROUP (N=32)	CONVENTIONAL-VENTILATION GROUP (N=32)
Patients with complications — no. (%)†	12 (38)	21 (66)
Patients with complications causing death in ICU — no.	9	15
No. of complications per patient‡	1.3	1.7
Death after discharge from ICU — no.	1	1
Complications — total no./no. causing death in ICU (% of group)§		
Myocardial infarction or cardiogenic shock	2/2 (6)	4/4 (12)
Sepsis¶	6/5 (19)	11/6 (34)
Renal failure	3/0 (9)	5/0 (16)
Pancreatitis	1/0 (3)	1/1 (3)
Polyneuropathy of the critically ill	0/0	1/0 (3)
Pneumonia‖	1/0 (3)	8/2 (25)§
Sinusitis‖	0/0	2/0 (6)
Pulmonary embolism	0/0	1/1 (3)
Massive blood loss	0/0	1/1 (3)
Infection at study entry**	2/2 (6)	0/0

*ICU denotes intensive care unit.

†P=0.02 for the comparison between the groups.

‡Only patients with complications were included in this calculation.

TABLE 3. CHARACTERISTICS OF PATIENTS ACCORDING TO THE SUCCESS OR FAILURE OF NONINVASIVE VENTILATION AND SURVIVAL OR DEATH IN THE CONVENTIONAL-VENTILATION GROUP.*

VARIABLE	NONINVASIVE-VENTILATION GROUP (N=32)			CONVENTIONAL-VENTILATION GROUP (N=32)		
	INTUBATION NOT REQUIRED (N=22)	INTUBATION REQUIRED (N=10)	P VALUE	SURVIVED (N=17)	DIED (N=15)	P VALUE
Age (yr)	47±21	62±7	0.006	51±20	65±14	0.03
SAPS†	12±4	16±3	0.009	10±4	14±4	0.02
Causes of acute respiratory failure						
Pneumonia (no.)	4	1		2	2	
Trauma (no.)	4	0		3	1	
Cardiogenic pulmonary edema (no.)	4	3		2	3	
Postoperative (no.)	10	6		10	9	
No. of invasive devices per patient	4±1	5±1	0.12	5±1	6±1	0.006
Initial improvement in PaO_2:FiO_2 (no.)	16	4	0.12	8	7	0.98
Sustained improvement in PaO_2:FiO_2 (no.)	17	2	0.003	16	8	0.01
Duration of mechanical ventilation (days)‡	2±1	15±7	<0.001	6±5	9±9	0.23
Length of stay in intensive care unit (days)§	6±6	16±7	0.002	18±21	12±12	0.28
Discharged from intensive care unit (no.)	22	1	<0.001	17	0	
Septic complications after study entry (no.)¶	1	5	0.006	5	6	0.53
Sepsis	1	1		5	0	
Severe sepsis	0	3		0	5	
Septic shock	0	1		0	1	

*Plus–minus values are means ±SD.

†SAPS denotes simplified acute physiologic score.[23] The range of possible values is 0 to 56.

‡For patients who underwent intubation after the failure of noninvasive ventilation, the duration of mechanical ventilation was the total period of ventilation.

§Patients who died in the intensive care unit are included. All complications listed occurred while patients were in the intensive care unit.

¶Causes of septic shock included necrotizing fasciitis (in the patient in the noninvasive-ventilation group) and pneumonia (in the patient in the conventional-ventilation group). Among the patients assigned to noninvasive ventilation who required intubation, all five patients who had septic complications died. Among the patients assigned to conventional ventilation, all patients who had severe sepsis or septic shock died.

Clinical trial –NIV vs MV

Method	Observational case control study
Participants	12 immunocompetent patient with ARDS without any distant organ failure.
Intervention	NIV ventilation
Comparator	12 intubated ARDSp patients matched for age, SAPS II, P/F and pH at admission
Outcome	Decreased cumulative time on ventilator (P=.0001) and ICU length of stay (P=.004). But no difference on mortality

Monaldi Arch Chest Dis. 2008 Mar;69(1):5-10

Clinical trial –NIV vs Oxygen

Method	Multicenter RCT
Participants	42 patients presented with acute onset respiratory distress with P/F >200 but <300 were randomized to receive NIV or oxygen.
Intervention	Patients were ventilated with bilevel positive pressure S/T mode. Tidal volume targeted between 6ml -10ml/kg .
Comparator	High flow oxygen through venturi mask
Outcome	Primary end point – ETI Secondary end point –ICU and hospital mortality

Table 1. Patient baseline characteristics

	Noninvasive Positive Pressure Ventilation, Group (n = 21)	Control Group (n = 19)	*p*
Age, mean (SD), yrs	43.8 ± 13.7	49.1 ± 13.7	.23
Male, no. (%)	16 (76.2)	8 (42.1)	.03
Smoking, no. (%)	5 (23.8)	7 (36.8)	.37
Height, mean (SD), cm	169 ± 6	167 ± 8	.21
Body mass index, mean (SD), kg/m^2	23.8 ± 2.8	22.9 ± 4.0	.39
Ideal body weight, mean (SD), kg	64.1 ± 7.2	60.6 ± 8.4	.17
Days since onset of acute lung injury, median (interquartile range)	2.0 (1.0–3.5)	3.0 (1.0–6.0)	.38
Underlying comorbidities, no. (%)			.71
Hypertension	4 (19.0)	7 (36.8)	.21
Immunosuppression[a]	5 (23.8)	6 (31.6)	.58
Diabetes mellitus	2 (9.5)	2 (10.5)	.92
Chronic renal insufficiency	1 (4.8)	4 (21.1)	.28
Cancer	0 (0.0)	1 (5.3)	.96
Causes of acute lung injury, no. (%)			
Pulmonary infection	10 (47.6)	10 (52.6)	
Acute pancreatitis	2 (9.5)	5 (26.3)	
Multiple trauma	3 (14.3)	0 (0)	
Sepsis[b]	3 (14.3)	3 (15.8)	
Others[c]	3 (14.3)	1 (5.3)	
Acute Physiology And Chronic Health Evaluation II score, mean (SD)	11.8 ± 6.3	13.4 ± 5.7	.39
Sequential Organ Failure Assessment score	3.9 ± 1.8	3.8 ± 2.1	.87
White blood cell count, $\times 10^9$/L, mean (SD)	15.6 ± 7.9	15.0 ± 15.1	.89
Neutrophil, $\times 10^9$/L, mean (SD)	82.8 ± 8.5	83.6 ± 6.4	.75
Hemoglobin, g/L, mean (SD)	125.2 ± 27.5	113.6 ± 31.2	.22

[a]Immunosuppression included drug-induced immunosuppression for solid organ transplants or as a result of corticosteroids or cytotoxic therapy; [b]sepsis and shock were defined by published criteria (26); [c]other causes for acute lung injury: drowning (two cases) and carbonic oxide poisoning (one case) in the noninvasive positive pressure ventilation group, hemorrhagic shock (one case) in the control group.

Table 3. Main outcomes

Outcome	Noninvasive Positive Pressure Ventilation Group (n = 21)	Control Group (n = 19)	*p*
Need for intubation, no. (%)	1 (4.8)	7 (36.8)	.02
Pulmonary infection	1	5	
Nonpulmonary infection	0	2	
Intubation, no. (%)	1 (4.8)	4 (21.1)	.04
Pulmonary infection	1	3	
Nonpulmonary infection	0	1	
Death, no. (%)			
Death in intensive care unit	1 (4.8)	5 (26.3)	.09
Death in hospital	1 (4.8)	5 (26.3)	.09
Days of intensive care, median (interquartile range)	5.9 (3.7–9.8)	7.8 (5.9–12.8)	.07
Days of hospital, median (interquartile range)	17.5 (11.3–22.8)	23.0 (10.8–34.3)	.48
Complications of invasive ventilation, no. (%)			
Ventilator-associated pneumonia[a]	0 (0.0)	1 (5.2%)	.29
Pulmonary barotrauma[b]	0 (0.0)	1 (5.2%)	.289
Abdominal-related sepsis[a]	1 (4.8)	4 (21.1)	.12
Organ failure, no. (%)			
Renal failure	1 (4.8)	2 (10.5)	.49
Cardiovascular failure	2 (9.5)	6 (31.6)	.12
Hepatic failure	0 (0.0)	2 (10.5)	.13
Hematologic failure	0 (0.0)	3 (15.8)	.06
Central nervous system failure	0 (0.0)	1 (5.2)	.29
Total	3 (14.3)	14 (73.7)	<.001

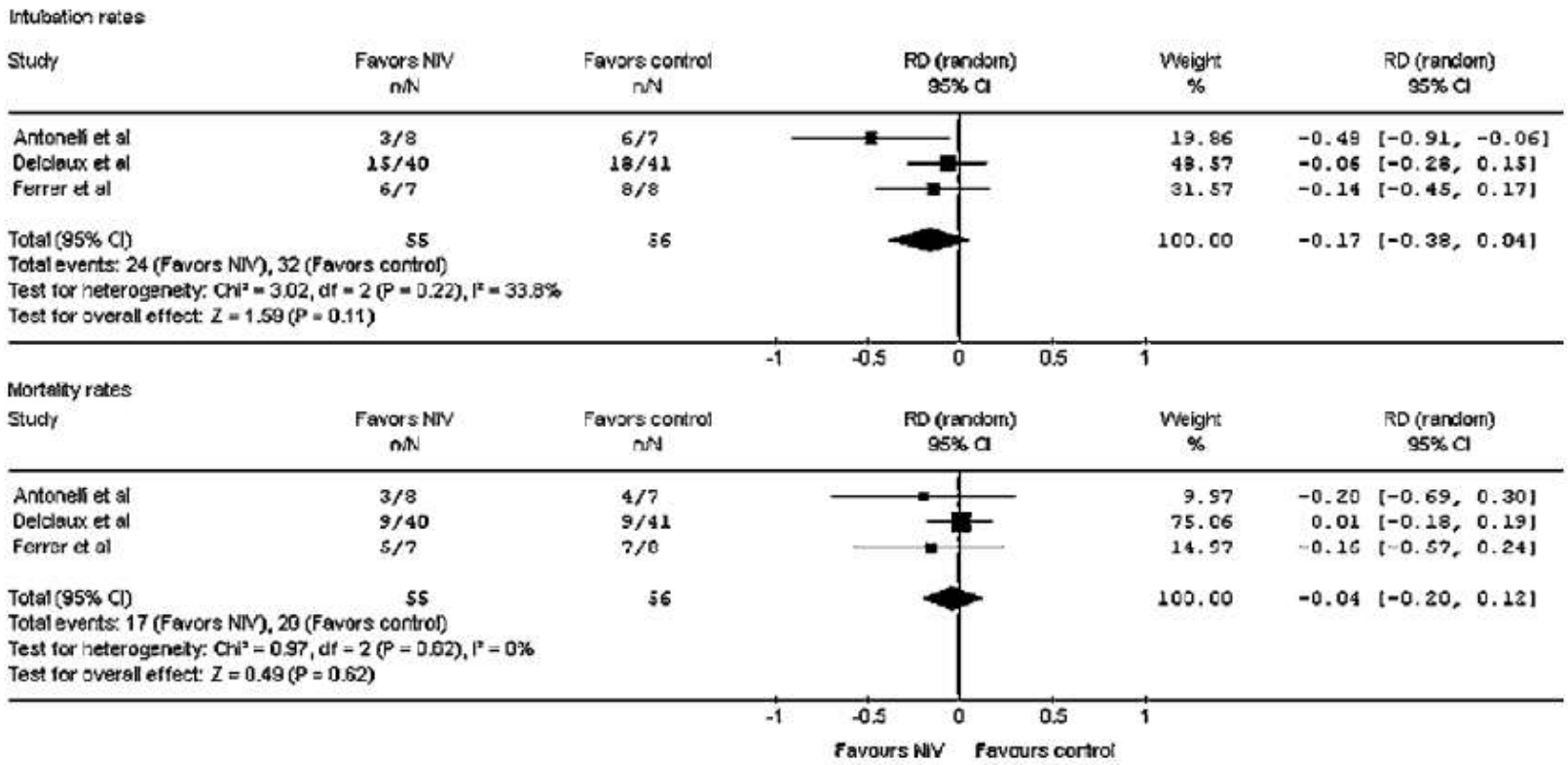
[a]Ventilator-associated pneumonia, abdominal-related sepsis, and organ failure were defined by published criteria (24, 27, 28); [b]pulmonary barotrauma included pneumothorax, subcutaneous emphysema, and mediastinal emphysema.

Crit Care Med 2012 Vol. 40, No. 2

Meta analysis -2006
R. Agarwal et al

Table 1 Randomized controlled trials employing noninvasive ventilation in acute respiratory distress syndrome.

Study	Ventilator	Mode	Interface	Pressure used, range (cm H_2O)
Antonelli et al.[7]	Conventional (Puritan Bennett 7200 ae, Siemens Servo 900C)	Bilevel positive airway pressure	Full face mask	IPAP: 14–20
Italy 1 center, ICU 15 patients Solid organ transplant				EPAP: 5–10
Delclaux et al.[8]	Non-conventional ventilator (VitalSigns)	Continuous positive airway pressure	Full face mask	7.5–10
France 6 centers, ICU 81 patients Heterogeneous				
Ferrer et al.[9]	Non-conventional ventilator (BiPAP Vision)	Bilevel positive airway pressure	Full face mask (if not tolerated—nasal mask)	IPAP: 10–24
Spain 1 center, ICU 15 patients Heterogeneous				EPAP: 4–12


Intubation rates
Study
Favors NIV n/N
Favors control n/N
RD (random) 95% CI
Weight %
RD (random) 95% CI
Antonelli et al 3/8 6/7 19.86 -0.48 [-0.91, -0.06]
Delclaux et al 15/40 18/41 48.57 -0.06 [-0.28, 0.15]
Ferrer et al 6/7 8/8 31.57 -0.14 [-0.45, 0.17]
Total (95% CI) 55 56 100.00 -0.17 [-0.38, 0.04]
Total events: 24 (Favors NIV), 32 (Favors control)
Test for heterogeneity: Chi² = 3.02, df = 2 (P = 0.22), I² = 33.8%
Test for overall effect: Z = 1.59 (P = 0.11)
-1 -0.5 0 0.5 1
Mortality rates
Study
Favors NIV n/N
Favors control n/N
RD (random) 95% CI
Weight %
RD (random) 95% CI
Antonelli et al 3/8 4/7 9.97 -0.20 [-0.69, 0.30]
Delclaux et al 9/40 9/41 75.06 0.01 [-0.18, 0.19]
Ferrer et al 5/7 7/8 14.97 -0.16 [-0.57, 0.24]
Total (95% CI) 55 56 100.00 -0.04 [-0.20, 0.12]
Total events: 17 (Favors NIV), 20 (Favors control)
Test for heterogeneity: Chi² = 0.97, df = 2 (P = 0.62), I² = 0%
Test for overall effect: Z = 0.49 (P = 0.62)
-1 -0.5 0 0.5 1
Favours NIV
Favours control

- Conclusion

This systematic review suggests that application of NIV in patients with ARDS does not decrease the rate of endotracheal intubation or ICU survival Thus NIV, if tried, should be tried under trial conditions, and as early as possible in patients with ARDS not responding to standard medical therapy

Meta analysis -2014

Table 1 Details of the six studies reviewed

First author, year	Population	Aetiology of ALI/ARDS	Interventions		NIPPV ventilator	NIPPV interface	NIPPV mode	Pressure range (cmH_2O)	Outcomes[†]
			Experimental group	Control group					
Antonelli *et al.* 2000[20]	15	Complicated pneumonia, extra-pulmonary sepsis, massive blood transfusion and acute pancreatitis	NIV	Standard treatment with supplemental oxygen administration	Puritan Bennett 7200 or Servo 990C Siemens	Full face mask	BiPAP	IPAP:14–20 EPAP:5–10	1.2
Delclaux *et al.* 2000[21]	81	Pneumonia, aspiration, near-drowning, SIRS, others	Oxygen therapy plus CPAP	Oxygen therapy alone	Vital Flow 100 CPAP Flow Generator	Full face mask	CPAP	CPAP:5–10	1.2.3
Auriant *et al.* 2001[22]	48	Interstitial pulmonary oedema, atelectasis, pneumonia	NPPV with standard treatment	Standard treatment with oxygen supplementation	BiPAP Vision; Respironics Inc.	Nasal mask	BiPAP	NM	1.3
Ferrer *et al.* 2003[23]	15	NM	NIV	Oxygen therapy with high concentration sources	BiPAP Vision; Respironics Inc.	Face mask or nasal mask	BiPAP	IPAP: 10–24 EPAP: 4–12	1.2
Zhan *et al.* 2012[24]	40	Pulmonary infection, acute pancreatitis, multiple trauma, sepsis, drowning, carbonic oxide poisoning, haemorrhagic shock	NPPV	High-concentration oxygen therapy	BiPAP Vision; Respironics Inc.	Face mask	BiPAP	IPAP: Tidal volume >6 mL/kg or reach the maximum tolerated level EPAP: 4–13	1.2.3
Zhi *et al.* 2012[25]	28	Severe pneumonia, trauma, severe acute pancreatitis, haemorrhagic shock, toxication, septic shock, others	NPPV	Oxygen therapy	BiPAP Vision	Full face mask	CPAP	CPAP: 8–16	1.2

Study or Subgroup	NIPPV Events	NIPPV Total	Standard Oxygen Therapy Events	Standard Oxygen Therapy Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Antonelli et al. 2000[20]	3	8	6	7	10.6%	0.44 (0.17–1.12)
Auriant et al. 2001[22]	5	24	12	24	19.9%	0.42 (0.17–1.00)
Delclaux et al. 2000[21]	15	40	18	41	29.5%	0.85 (0.50–1.45)
Ferrer et al. 2003[23]	6	7	8	8	13.3%	0.86 (0.60–1.24)
Zhan et al. 2012[24]	1	21	4	19	7.0%	0.23 (0.03–1.85)
Zhi et al. 2012[25]	5	15	11	13	19.6%	0.39 (0.19–0.84)
Total (95% CI)		**115**		**112**	**100.0%**	**0.59 (0.44–0.80)**
Total events	35		59			

Heterogeneity: $\chi^2 = 8.82$, df = 5 ($P = 0.12$); $I^2 = 43\%$

Test for overall effect: $z = 3.44$ ($P = 0.0006$)

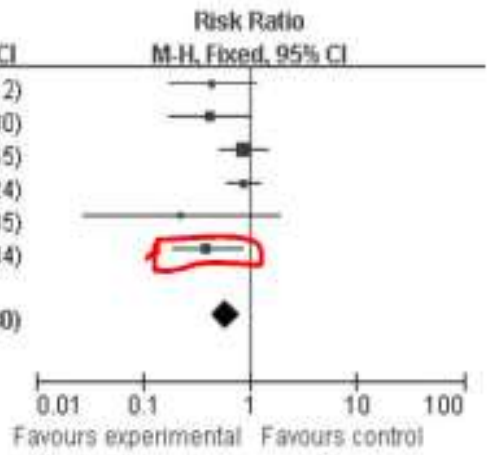


Figure 2 Endotracheal intubation rate: NIPPV versus standard oxygen therapy. CI, confidence interval; M.-H., Mantel-Haenszel; NIPPV, non-invasive positive pressure ventilation.

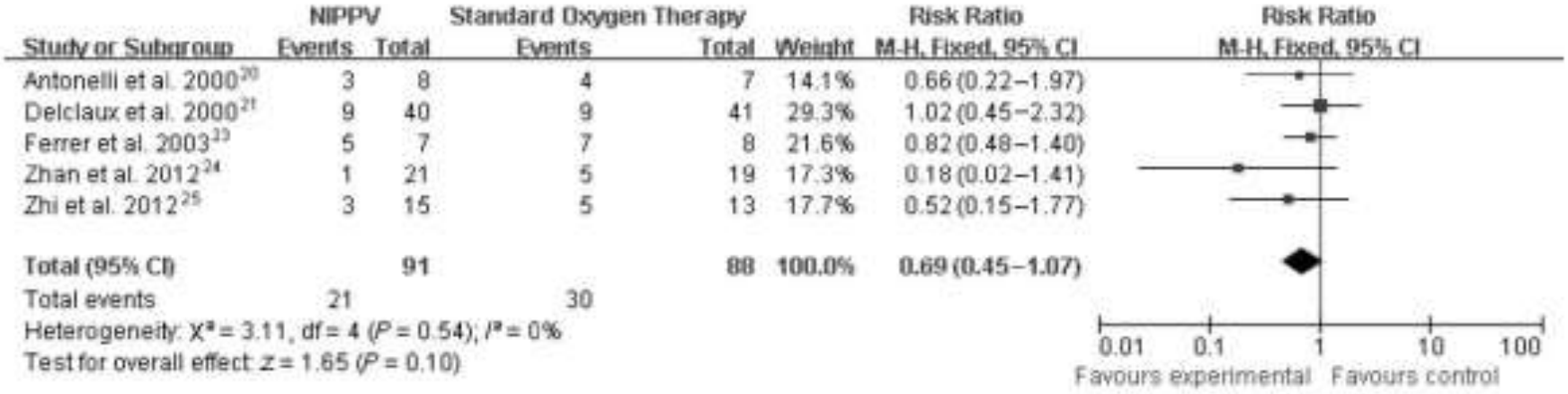


Figure 3 ICU mortality rate: NIPPV versus standard oxygen therapy. CI, confidence interval; ICU, intensive care unit; M.-H., Mantel-Haenszel; NIPPV, non-invasive positive pressure ventilation.

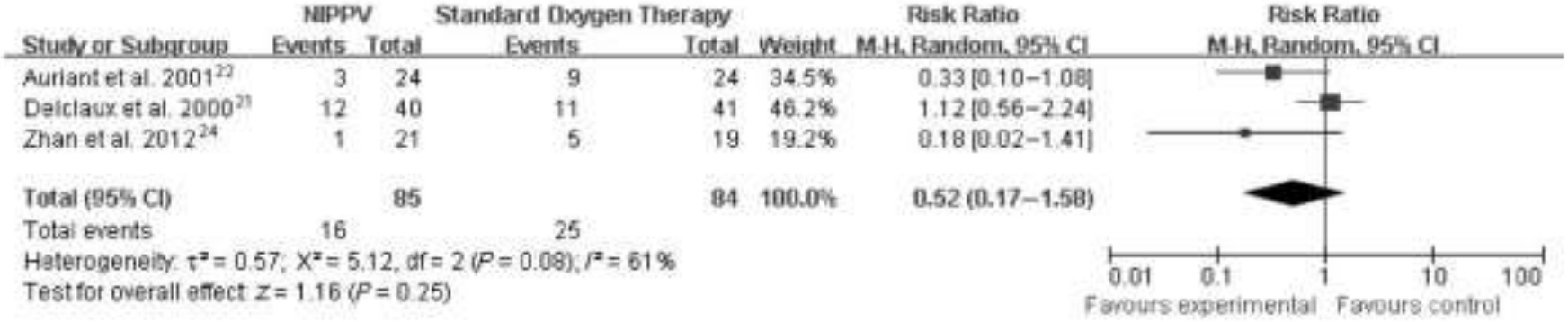


Figure 4 Hospital mortality rate: NIPPV versus standard oxygen therapy. CI, confidence interval; M.-H., Mantel-Haenszel; NIPPV, non-invasive positive pressure ventilation.

- Conclusion

the early use of NIPPV can decrease the endotracheal intubation rate in patients with ALI/ARDS, but does not change the mortality of these patients .

Real life scenario –indian data

Study (year)	R Agarwal et al(2009)	ISS et al (2015)	R Chawla et al (2015)
Design	Prospective observational study	Prospective observational study	Prospective observational cohort study
Participant	40 patients with AHRF (P/F<300).	41 patients with ARDS (as per AECC criteria but patients with P/F </=100 excluded)	96 patients with ARDS (as per Berlin definition)
Intervention	Bilevel PAP Through a portable NIV with full face mask	NIV using a full face mask through an ICU ventilator	NIV using a full face mask through an ICU ventilator
comparator	None	None	Patient with ARDS who were intubated at the outset

Primary outcome	ETI rate/NIV failure	ETI rate/NIV failure	ETI rate /NIV failure
Result	•ETI was required in 47.5% of overall population. •57.1% of patients with ARDS and 36.9% of patients with AHRF due to other causes required intubation. •Only factor predicting NIV failure was baseline P/F ratio.	• NIV failure occurred in 56% •Admission APACHE II >17 and failure to improve P/F more than 150 were independent predictors of NIV failure	•NIV failure defined as ETI was seen in 43.8%. •NIV failure was significantly higher in moderate/sever ARDS. •Predictors of failure on multivariate analysis were ➢ presence of septic shock ➢Severity of ARDS ➢ low P/F ratio • LOS in ICU and hospital LOS was significantly less in ARDS patient treated initially on NIV than IMV group •Extrapulmonary ARDS was predominant population

Table 6. Univariate Analysis of Factors Predicting Failure of Noninvasive Ventilation

	NIV Success (n = 21)	NIV Failure (n = 19)	Crude Odds Ratio	95% Confidence Interval	P
ALI/ARDS (n, %)	7 (33.3)	12 (63.2)	0.44	0.12–1.6	.20
Underlying immunosuppression (n, %)	8 (38.1)	11 (57.9)	2.23	0.63–7.93	.21
APACHE II score (mean ± SD)	14.8 ± 4.4	15 ± 3.5	1.02	0.87–1.19	.85
Baseline P_{aO_2}/F_{IO_2} (mean ± SD mm Hg)	144.2 ± 48.6	103.8 ± 33.1	0.97	0.95–0.99	.01
Change in Respiratory Rate (mean ± SD breaths/min)					
Hour 0 to hour 1	−10.3 ± 4.7	−8.2 ± 4.9	1.04	0.95–1.13	.40
Hour 0 to hour 4	−12.9 ± 7.5	−10.9 ± 7.6	1.10	0.96–1.27	.17
Change in P_{aO_2} (mean ± SD mm Hg)					
Hour 0 to hour 1	17.7 ± 25.5	26.5 ± 31.6	0.99	0.97–1.01	.33
Hour 0 to hour 4	23.7 ± 26.1	13.3 ± 21.4	0.98	0.95–1.01	.18

NIV = noninvasive ventilation
ALI = acute lung injury
ARDS = acute respiratory distress syndrome
APACHE = Acute Physiology and Chronic Health Evaluation
F_{IO_2} = fraction of F_{IO_2}

Comparison of patients as per the severity of ARDS classified as per the Berlin definition

	Mild (n = 59)	Moderate (n = 71)	Severe (n = 40)	*P* value
Age, y (±SD)	48.6 (±16)	45.9 (±17.5)	49 (±15.8)	.551
Sex, male (%)	31 (52.5%)	44 (62%)	30 (75%)	.078
APACHE II score	14 (±7.3)	17.7 (±7)	21.9 (±9.4)	.000*
H1N1 infection (%)	13 (22%)	19 (26.8%)	16 (40%)	.210
Septic shock (%)	19 (32.2%)	40 (56.3%)	24 (60%)	.006*
SOFA score	5.2 (±4.4)	9.1 (±4.6)	10.2 (±3.4)	.000*
Cause of ARDS				.252
Pulmonary (%)	34 (57.6%)	42 (59.2%)	24 (60%)	
Extrapulmonary (%)	23 (39%)	23 (32.4%)	10 (25%)	
Both (%)	2 (3.4%)	6 (8.5%)	6 (15%)	
ICU LOS, d	10.6 (±9.5)	11.7 (±9.2)	11 (±7.8)	.770
Hospital LOS, d	15.9 (±13.4)	16.4 (±12.4)	14 (±9.2)	.588
Pao_2/Fio_2	226.7 (±21.8)	148.3 (±30)	78.9 (±50.6)	.000*
ICU mortality	12 (20.3%)	33 (46.5%)	18 (45%)	.004*

* Indicates statistically significant.

R. Chawla et al. / Journal of Critical Care 31 (2016) 26–30

European data

Method	Prospective observational study
Participants	Patients admitted with ARDS in 3 European ICU between 2004 -2007 who fulfill the inclusion and exclusion criteria
Intervention	As per protocol eligible patients received bi-level positive pressure ventilation via different interfaces.
Outcome	Primary outcome variable was percentage of patient received NIV, intubation rate and predictors of NIV failure. Secondary outcome variables were nosocomial infection, ventilation days length of ICU stay, survival of ICU and hospital admission

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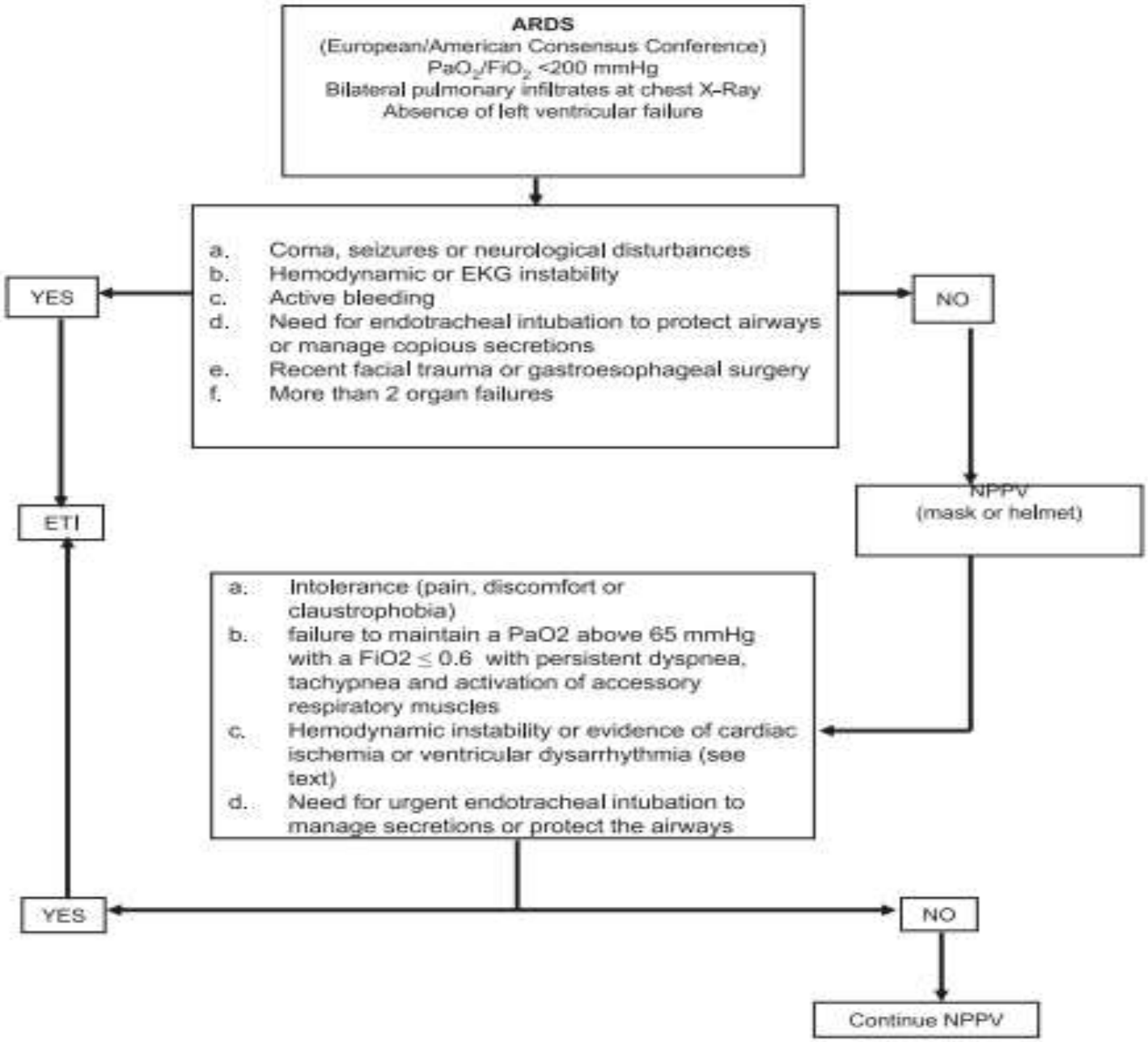

ARDS
(European/American Consensus Conference)
PaO_2/FiO_2 <200 mmHg
Bilateral pulmonary infiltrates at chest X-Ray
Absence of left ventricular failure
a. Coma, seizures or neurological disturbances
b. Hemodynamic or EKG instability
c. Active bleeding
d. Need for endotracheal intubation to protect airways or manage copious secretions
e. Recent facial trauma or gastroesophageal surgery
f. More than 2 organ failures
YES
NO
ETI
NPPV
(mask or helmet)
a. Intolerance (pain, discomfort or claustrophobia)
b. failure to maintain a PaO2 above 65 mmHg with a FiO2 ≤ 0.6 with persistent dyspnea, tachypnea and activation of accessory respiratory muscles
c. Hemodynamic instability or evidence of cardiac ischemia or ventricular dysarrhythmia (see text)
d. Need for urgent endotracheal intubation to manage secretions or protect the airways
YES
NO
Continue NPPV

Table 2. Outcome variables and complications after study entry

	Avoided Intubation (n = 79)	Required Intubation (n = 68)	*p* Value
Outcome variables			
Improvement of gas exchange after 1 hr, n (%)	32 (41)	20 (29)	.21
Sustained improvement of gas exchange, n (%)	59 (75)	12 (18)	<.001
Duration of NPPV (hrs) without discontinuation, median (25th–75th)	42 (24–51)	24 (21–47)	.002
ICU length of stay (days), median (25th–75th)	6 (3–11)	7 (3–18)	.24
Skin breakdown, n (%)	8 (10)	9 (13)	.32
ICU mortality, n (%)	5 (6)	36 (53)	<.001
Hospital mortality, n (%)	15 (19)	38 (54)	<.01
Complications after study entry, n (%)			
None	58 (73)	19 (28)	<.001
Sepsis	13 (16)	19 (28)	.11
Severe sepsis or septic shock	6 (7)	16 (23)	.01
Ventilator-associated pneumonia	2 (2)	14 (20)	.001

Variable	Avoided Intubation, Mean (SD) (n = 79)	Required Intubation, Mean (SD) (n = 68)	*p* Value	Threshold Value[a]	AUC ± SE	95% CI	Sensitivity (95% CI)	Specificity (95% CI)
Pa_{O_2}/F_{IO_2} basal	116 (38)	105 (33)	.06	≤102	0.61 ± 0.04	0.52–0.69	0.6 (0.48–0.72)	0.66 (0.54–0.76)
Pa_{O_2}/F_{IO_2} after 1 hr	195 (66)	168 (48)	.009	≤175	0.61 ± 0.04	0.53–0.69	0.59 (0.46–0.71)	0.65 (0.53–0.75)
pH basal	7.41 (0.08)	7.39 (0.08)	.21	≤7.45	0.59 ± 0.04	0.51–0.67	0.87 (0.76–0.94)	0.37 (0.26–0.48)
pH after 1 hr	7.42 (0.06)	7.39 (0.06)	.02	≤7.37	0.61 ± 0.04	0.53–0.69	0.63 (0.51–0.75)	0.63 (0.52–0.74)
RR, basal breaths/min	35 (5)	36 (5)	.27	>31	0.54 ± 0.04	0.46–0.62	0.9 (0.8–0.96)	0.25 (0.16–0.36)
RR after 1 hr, breaths/min	27 (5)	30 (7)	.0006	>29	0.67 ± 0.04	0.59–0.75	0.63 (0.51–0.75)	0.67 (0.56–0.77)
Pa_{CO_2} basal, mm Hg	40 (13)	40 (13)	.91	>34	0.51 ± 0.04	0.43–0.59	80.6 (69–89)	27.8 (18.3–39)
Pa_{CO_2} after 1 hr, mm Hg	39 (8)	41 (13)	.46	>36	0.53 ± 0.04	0.44–0.61	0.48 (0.36–0.61)	0.71 (0.6–0.81)
Δ Pa_{O_2}/F_{IO_2}	85 (63)	65 (56)	.05	≤98	0.56 ± 0.04	0.48–0.64	0.84 (0.73–0.92)	0.3 (0.2–0.42)
Δ pH	0.0013 (0.0634)	−0.0051 (0.059)	.52	≤0.08	0.53 ± 0.04	0.44–0.61	0.22 (0.13–0.34)	0.89 (0.79–0.95)
Δ RR, breaths/min	8 (6)	6 (7)	.02	≤4	0.64 ± 0.04	0.55–0.71	0.53 (0.4–0.65)	0.72 (0.61–0.82)
Δ Pa_{CO_2}, mm Hg	0.71 (8)	−1.35 (14)	.26	>3	0.54 ± 0.04	0.46–0.66	0.69 (0.57–0.8)	0.43 (0.32–0.55)

- In a survey of NIV use in a tertiary care hospital in North India P/F ratio </= 146 after 1 hour of NIV in AHRF shown to have better specificity than P/F </= 175

Table 5. Impact of P_{aO_2}/F_{IO_2} Scores at 1 Hour and Outcome in Subjects Receiving NIV*

	Hypoxemic Respiratory Failure			Hypercapnic Respiratory Failure		
	Success (n = 14)	Failure (n = 24)	P	Success (n = 33)	Failure (n = 23)	P
P_{aO_2}/F_{IO_2}, mm Hg						
≤ 146	2 (14.3)	16 (66.7)	.003	7 (21.2)	3 (13)	.50
> 146	12 (85.7)	8 (33.3)		26 (78.8)	20 (87)	
≤ 175	4 (28.6)	18 (75)	.008	13 (39.4)	9 (39.1)	.99
> 175	10 (71.4)	6 (25)		20 (60.6)	14 (60.9)	

Values are no. (%).

* Data of 94 applications as subjects were intubated within an hour during 7 instances of noninvasive ventilation (NIV) administration.

Table 6. Outcome Parameters During the ICU Course of the 2 Groups Receiving 101 NIV Applications

Conclusion

- Proper patient selection and early identification of NIV failure may be the keys of NIV success in ARDS.
- NIV may avoid intubation but it should not be considered as an alternative to intubation.

NIV in immunosuppressed

- Recommendation
  - ✓ NIV is recommended early in the course of hypoxic respiratory failure in immunocomprmised patients, particularly in those with hematological malignancies.

    Indian J Crit Care Med April-June 2006 Vol 10 Issue 2

  - ✓ We suggest that noninvasive positive pressure ventilation be used for immunosuppressed [defined as patient on immunosupressive chemotherapy or bone marrow or solid organ transplant recipient) patients who have acute respiratory failure (grade 2B recommendation).

    CMAJ, February 22, 2011, 183(3)

Evidences

Method	Single center RCT non blinded
Participants	52 immunosuppressed patient with pulmonary infiltrate , fever and moderate respiratory failure (defined as dyspnea at rest, RR>30, P/F<200) Exclusion –GCS<8, COPD, CCF, MOF, shock
Intervention	Intermittent NIV (alternated every 3 hr, at least for 45 minutes during each session) through a full face mask.
Comparator	Standard medical therapy with supplemental oxygen through venturi.
Outcome	Primary – intubation (as per predefined criteria)

(N Engl J Med 2001;344:481-7.)

Types of immunosuppression — no. (%)		
Hematologic cancer and neutropenia	15 (58)	15 (58)
Bone marrow transplantation	8 (31)	9 (35)
High-dose chemotherapy	7 (27)	6 (23)
Drug-induced immunosuppression	9 (35)	9 (35)
Organ transplantation	3 (12)	4 (15)
Corticosteroid therapy	4 (15)	3 (12)
Other	2 (8)	2 (8)
Acquired immunodeficiency syndrome	2 (8)	2 (8)

TABLE 2. OUTCOMES OF TREATMENT.*

OUTCOME	NONINVASIVE-VENTILATION GROUP (N=26)	STANDARD-TREATMENT GROUP (N=26)	P VALUE	RELATIVE RISK (95% CI)
Intubation — no./total no. (%)	12/26 (46)	20/26 (77)	0.03	0.60 (0.38–0.96)
Immunosuppression from hematologic cancer and neutropenia	8/15 (53)	14/15 (93)	0.02	0.57 (0.35–0.93)
Drug-induced immunosuppression	3/9 (33)	5/9 (56)	0.32	0.60 (0.20–1.79)
Immunosuppression from the acquired immunodeficiency syndrome	1/2 (50)	1/2 (50)	0.83	1.00 (0.14–7.10)
Initial improvement in PaO_2:FiO_2 — no. (%)	12 (46)	4 (15)	0.02	
Sustained improvement in PaO_2:FiO_2 without intubation — no. (%)	13 (50)	5 (19)	0.02	
Death in the ICU — no./total no. (%)†	10/26 (38)	18/26 (69)	0.03	0.56 (0.32–0.96)
Immunosuppression from hematologic cancer and neutropenia	7/15 (47)	13/15 (87)	0.02	0.54 (0.30–0.96)
Drug-induced immunosuppression	3/9 (33)	4/9 (44)	0.50	0.75 (0.23–2.44)
Immunosuppression from the acquired immunodeficiency syndrome	0/2	1/2 (50)	0.50	0.50 (0.13–2.00)
Total duration of any ventilatory assistance — days				
Among all patients	6±3	6±5	0.59	
Among survivors	5±2	3±5	0.12	
Length of ICU stay — days				
Among all patients	7±3	9±4	0.11	
Among survivors	7±3	10±4	0.06	
Death in the hospital — no./total no. (%)	13/26 (50)	21/26 (81)	0.02	0.62 (0.40–0.95)
Immunosuppression from hematologic cancer and neutropenia	8/15 (53)	14/15 (93)	0.02	0.57 (0.35–0.93)
Drug-induced immunosuppression	4/9 (44)	6/9 (67)	0.32	0.67 (0.28–1.58)
Immunosuppression from the acquired immunodeficiency syndrome	1/2 (50)	1/2 (50)	0.83	1.00 (0.14–7.10)

NIV in solid organ transplant recepient JAMA 2002

Method	Prospective RCT
Participant	40 SOT recipients with acute respiratory failure defined as P/F<200 and RR >35 randomized for intervention or control
Intervention	Bilelvel NIV via full face mask with standard medical care
Comparator	Supplementary oxygen starting at FiO2.4 with target spo2 >90% via venturi
Outcome	Primary outcome was to measure ETI rate. Secondary outcomes include any complication, ICU and hospital mortality.

Table 1. Baseline Characteristics of the Patients and Causes of Acute Respiratory Failure*

	Noninvasive Ventilation Group (n = 20)	Standard Treatment Group (n = 20)	*P* Value
Age, y	45 (19)	44 (10)	.89
No. (%) of men	13 (65)	12 (60)	.50
Simplified Acute Physiologic Score	13 (4)	13 (3)	.93
No. of invasive devices per patient	5 (1)	5 (1)	.90
Heart rate, beats/min	96 (20)	101 (14)	.38
Respiratory rate, breaths/min	38 (3)	37 (1)	.32
Body temperature, °C	37.2 (0.9)	37 (0.7)	.35
White blood cells, $\times 10^9$/L	0.005 (0.002)	0.007 (0.005)	.12
No. (%) of infections prior to entry	8 (40)	9 (45)	.19
Systolic blood pressure, mm Hg	135 (23)	140 (24)	.53
Arterial pH	7.46 (0.05)	7.43 (0.04)	.13
$Paco_2$, mm Hg	42 (10)	38 (9)	.14
No. (%) of patients with $Paco_2$ >45 mm Hg	7 (35)	3 (15)	.13
Ratio of Pao_2 to fraction of inspired oxygen	129 (30)	129 (30)	.96
No. (%) of patients who received an organ transplant			
Liver	10 (50)	12 (60)	.37
Lung	4 (20)	2 (10)	.33
Kidney	6 (30)	6 (30)	.63
Time from transplantation, d†	23 (14)	22 (15)	.88
Causes of acute respiratory failure‡			
Pneumonia	2 (10)	2 (10)	.69
Cardiogenic pulmonary edema	4 (20)	5 (25)	.50
Acute respiratory distress syndrome§	8 (40)	7 (35)	.50
Mucous plugging or atelectasis	5 (25)	5 (25)	.64
Pulmonary embolism	1 (5)	1 (5)	.75

Table 2. Outcome Variables*

Variable	Noninvasive Ventilation Group (n = 20)	Standard Treatment Group (n = 20)	*P* Value
Initial improvement in ratio of PaO_2 to fraction of inspired oxygen	14 (70)	5 (25)	.005
Sustained improvement in ratio of PaO_2 to fraction of inspired oxygen, without intubation	12 (60)	5 (25)	.03
Patients intubated within 24 h of study entry	3 (15)	10 (50)	.02
Patients requiring intubation	4 (20)	14 (70)	.002
Failures per subgroup of patients			
Acute respiratory distress syndrome (pulmonary etiology)†	2/5 (40)	2/2 (100)	.28
Acute respiratory distress syndrome (extrapulmonary etiology)†	1/3 (33)	4/5 (80)	.28
Pneumonia†	1/2 (50)	1/2 (50)	.83
Cardiogenic pulmonary edema†	0/4 (0)	5/5 (100)	.007
Pulmonary embolism	0/1 (0)	0/1 (0)	.99
Mucous plugging or atelectasis†	0/5 (0)	2/5 (40)	.22
Duration of mechanical ventilation, d‡§	4 (5)	5 (6)	.58
Duration of mechanical ventilation in survivors, d‡	2 (0.7)	1.6 (2)	.50
Duration of use for all invasive devices present at study entry, d‡	5 (5)	9 (6)	.05
Length of intensive care unit stay, d‡	7 (5)	10 (6)	.18
Length of intensive care unit stay in survivors, d‡	5.5 (3)	9 (4)	.03
Intensive care unit deaths‖	4 (20)	10 (50)	.05
Intensive care unit deaths per subgroup of patients†			
Acute respiratory distress syndrome	3/8 (37)	4/7 (57)	.40
Pneumonia	1/2 (50)	1/2 (50)	.80
Cardiogenic pulmonary edema	0/4 (0)	4/5 (80)	.04
Pulmonary embolism	0/1 (0)	0.1 (0)	.99
Mucous plugging or atelectasis	0/5 (0)	1/5 (20)	.50
Hospital deaths¶	7 (35)	11 (55)	.17

* Values are expressed as number (percentage) unless otherwise indicated.

Method	Prospective case control study
Participants	24 patients admitted in ICU with AIDS (defined as per CDC criteria) with PCP; and in respiratory failure
Intervention	NIV with bilevel positive airway pressure through a full face mask using time cycled mode
Comparator	24 patients with AIDS and PCP infection intubated in emergency or intubated outside within 24 hr prior to ICU admission. Matching was done at various points with study cohort
Outcome	The primary outcome variable was crude ICU survival rate.

Intensive Care Med (2002) 28:1233–1238
DOI 10.1007/s00134-002-1395-2

	Noninvasive ventilation (n=24)	Conventional ventilation (n=24)	P value
Age, years*	37±9	36±8	0.68
PaO_2:FiO_2, mm Hg*	122±44	121±40	0.93
CD4+, cells/mm*	21±13	19±18	0.66
SAPS II score*	37±9	38±5	0.63
SOFA score*	6.8±2	6.7±3	0.89
Weight, kg	57±11	59±13	0.56
Height, cm	170±9	168±8	0.42
Hematocrit, %	32±7	31±5	0.57
LDH, U/l	1396±433	1511±592	0.44
$PaCO_2$, mm Hg	29±7	32±6	0.11
pH	7.44±0.06	7.43±0.05	0.53
Respiratory rate, bpm	35±7	37±8	0.36
Mean blood pressure, mm Hg	80±11	76±11	0.21

Table 2 Outcome variables in NPPV and conventional ventilation groups

	Noninvasive ventilation	Conventional ventilation	*P* value
Number of invasive devices (mean ± SD)	2±2	5±0	0.0001
Pneumothorax	2 (8.3%)	9 (38%)	0.033
Positive blood cultures	2 (8%)	7 (29%)	0.133
Septic shock	6 (25%)	13 (54%)	0.078
Nurse workload*	7.8±1.9	8.2±1.2	0.388
Duration of mechanical ventilation, days	6±2	7±1	0.034
Duration of ICU stay, days	7±4	10±4	0.013
Duration of hospital stay, days	13±5	24±17	0.004
SOFA score on study day 7*	5.7±1.4	6.5±1.94	0.072
ICU survival	75%	38%	0.022
2-month survival	58%	21%	0.020
6-month survival	25%	16%	0.678

*Daily nursing assistance was recorded on the first 3 days of the study following a previously described visual analogic scale [23]

Design	Retrospective analysis of prospectively collected data between 2002 and 2006
Participants	1302 patients of hematological malignancy admitted in 158 Italian ICU with acute respiratory failure.
Objective	Mortality (intensive care unit and hospital) was assessed in patients treated initially with noninvasive mechanical ventilation vs. invasive mechanical ventilation and in those treated with invasive mechanical ventilation *ab initio* vs. after noninvasive mechanical ventilation failure.
Result	Only 21% of the patients received NIV initially, 46% of them later required IMV. High organ failure score and ALI/ARDS present at the the onset are the predictors of NIMV failure on multivariate regression. While successful NIMV was statistically collaborating with sucessful outcome. Delayed vs immediate ETI i.e. at ICU admission did not increase mortality significantly.

Crit Care Med 2011; 39:2232–2239

Table 3. Comparison of the successful and unsuccessful noninvasive mechanical ventilation groups

Group Characteristics	Successful NIMV (n = 147 [54%])	Unsuccessful NIMV (n = 127 [46%])	*p*
Males–no. (%)	83 (56)	79 (63)	.30
Mean Age (SD), yrs	60 (17)	60 (14)	.73
Mean Simplified Acute Physiology Score II (SD)	47 (17)	51 (15)	.07
Median Glasgow Coma Scale (interquartile range)	15 (14–15)	15 (14–15)	.95
ALI-ARDS at Admission–no. (%)			
ALI	21 (14)	36 (28)	<.01
ARDS	15 (10)	17 (13)	.41
Infections[a]–no. (%)			
Present at ICU admission	46 (31)	42 (33)	.60
Onset during ICU stay	1 (1)	19 (15)	<.0001
Organ Failure–no. (%)			
Present at ICU admission	141 (96)	121 (95)	.80
Onset during ICU stay	40 (27)	80 (63)	.00005
Mean Duration of Care (SD)–days			
Total hospital stay	29 ± 24	32 ± 30	.39
ICU stay	6 ± 5	14 ± 12	<.0001
Duration of NIMV	5 ± 4	3 ± 3	<.0001
Mortality–no. (%)			
ICU mortality			
All patients	28 (19)	78 (61)	<.0001
Patients with ALI or ARDS	13 of 36 (36)	39 of 53 (74)	.0005
Hospital mortality			
All patients	50 (34)	83 (65)	<.0001
Patients with ALI or ARDS	15 of 36 (42)	41 of 53 (77)	.001

ALI, acute lung injury; ARDS, adult respiratory distress syndrome; ICU, intensive care unit; NIMV, noninvasive mechanical ventilation.

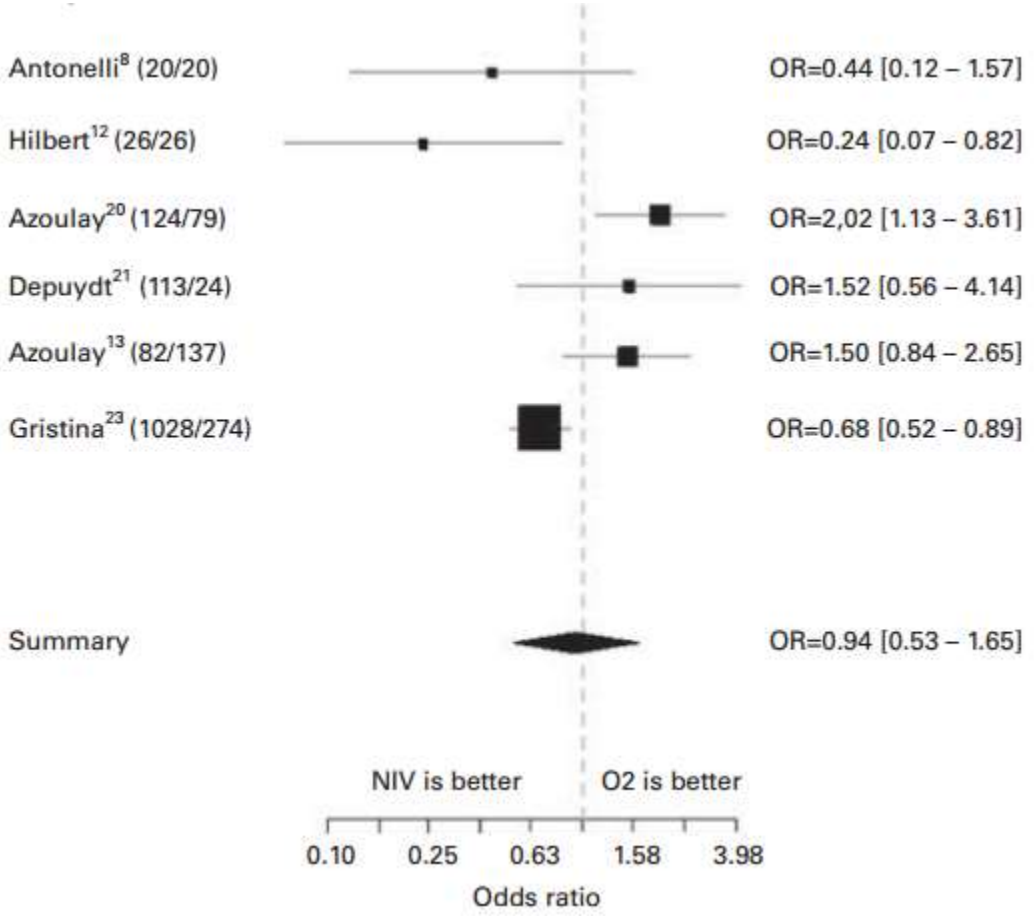
[a]Information on infections was available only for 768 patients admitted during 2005–2006 (591 invasive mechanical ventilation group, 177 NIMV group).

Table 4. Comparison of invasive mechanical ventilation and unsuccessful noninvasive mechanical ventilation groups

Group Characteristics	Invasive Mechanical Ventilation (n = 1028 [79%])	Unsuccessful Noninvasive Mechanical Ventilation (n = 127 [46%])	*p*
Males–no. (%)	602 (59)	79 (63)	.44
Mean Age (SD), yrs	64 (15)	60 (14)	<.01
Mean Simplified Acute Physiology Score II (SD)	58 (18)	51 (15)	<.0001
Median Glasgow Coma Score (interquartile range)	10 (7–15)	15 (14–15)	<.0001
Organ Failure at Admission	1002 (97)	121 (95)	.16
ALI–ARDS at Admission–no. (%)			
ALI	110 (11)	36 (28)	<.0001
ARDS	89 (9)	17 (13)	.08
Infections–no. (%)[a]			
Present at ICU admission	228 (39)	42 (52)	.02
Onset during ICU stay	122 (21)	19 (23)	.56
Organ Failure–no. (%)			
Present at ICU admission	1002 (97)	121 (95)	.16
Onset during ICU stay	434 (42)	80 (63)	<.0001
Mean Duration of Care (SD)–days			
Total hospital stay	29 (36)	32 (30)	.44
ICU stay	12 (16)	14 (12)	.27
Duration of mechanical ventilation	11 (13)	10 (11)	.63
Mortality–no. (%)			
ICU mortality			
All patients	511 (50)	78 (61)	.01
Patients with ALI or ARDS	119 of 199 (60)	39 of 53 (74)	.07
Hospital mortality			
All patients	597 (58)	83 (65)	.12
Patients with ALI or ARDS	137 of 199 (69)	41 of 53 (77)	.23
Mortality after ICU stay	88 (17)	5 (10)	.22

ALI, acute lung injury; ARDS, adult respiratory distress syndrome; ICU, intensive care unit

NIV in hematological maligancy



Bone Marrow Transplantation (2012) 47, 469–472

Conclusion

- NIV is helpful in selected subgroup of immunosuppressed patient with AHRF.
- Predictors of NIV failure in immunosuppressed should be looked for
  - ✓ Higher illness severity at baseline reflected by SAPS II
  - ✓ Higher RR under NIV
  - ✓ Later initiation of NIV after ICU admission
  - ✓ Need for vasopressors
  - ✓ Need for RRT
  - ✓ Presence of ALI /ARDS

Curr Opin Crit Care 2012, 18:54–60

NIV in post operative respiratory failure

- Post operative pulmonary complication [PPC] may be seen in 5-10% of all surgeries and 9-40% of abdominal surgeries.
- PPC can be of diverse etiology related or unrelated to index surgery and they can increase hospital LOS, cost, morbidity and mortality significantly.
- NIV has now been evaluated widely for prvention and/or therapy of PPC

Intensive Care Med (2011) 37:918–929

- Recommendation
  - ❑ Continuous positive airway pressure be used in patients who have respiratory failure after abdominal surgery (grade 2C recommendation)
  - ❑ Noninvasive positive pressure ventilation to be used in patients who have respiratory failure after lung-resection surgery(grade 2C recommendation).

CMAJ, February 22, 2011,183(3)

- ✓ NIV has been used in a variety of other conditions (such as acute respiratory distress syndrome, postoperative and posttransplantation respiratory failure) with reduced intubation rates, ICU stay and mortality. In this context, patients who would be considered for intubation if NIV fails should only receive NIV in ICU. [D]

Thorax 2002;57:192–211

- ✓ NIV may be used in patients who develop respiratory distress or respiratory failure after lung resection or abdominal surgery. (level II)

Indian J Crit Care Med April-June 2006 Vol 10 Issue 2

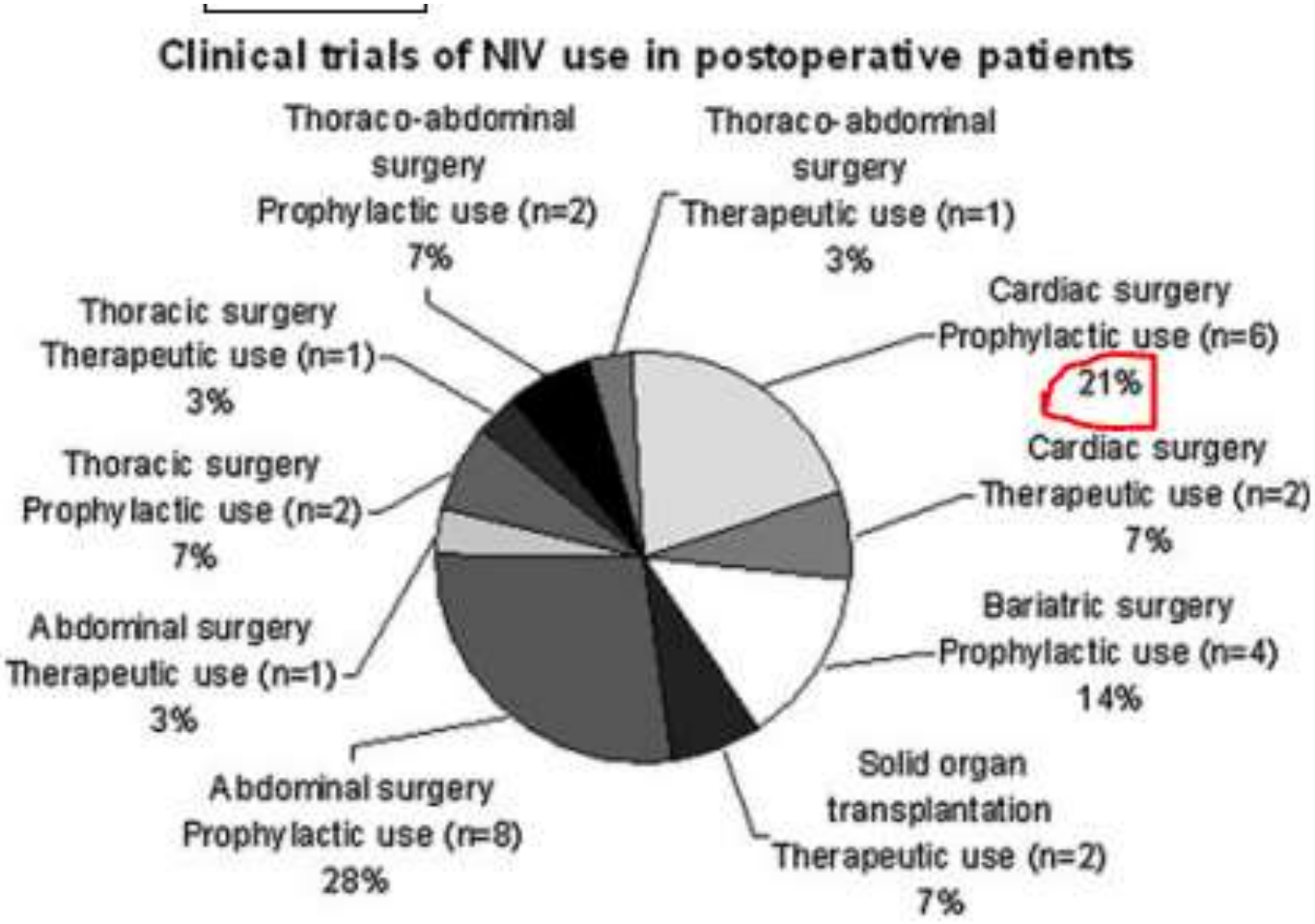


Fig. 1 Total number and percentage of the available studies of NIV in postoperative patients

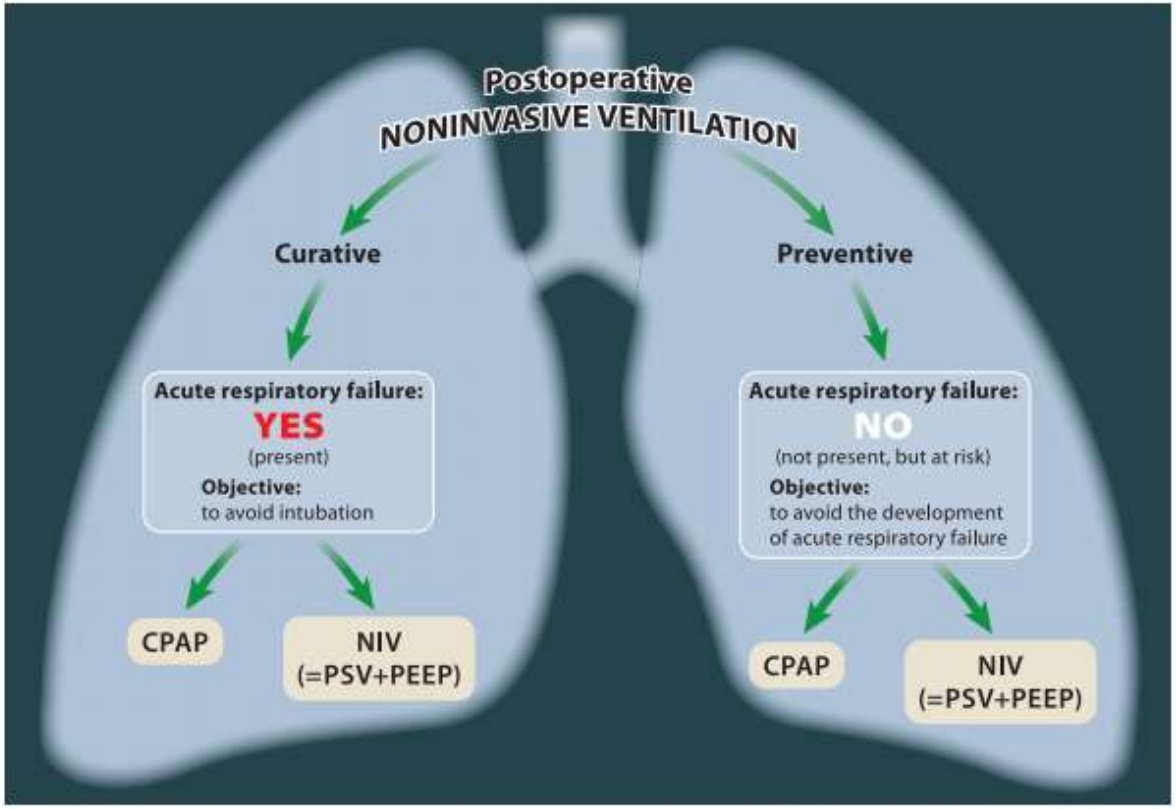


Fig. 1. The two main strategy approaches for applying postoperative noninvasive ventilation (NIV). CPAP = continuous positive airway pressure; PSV = pressure support ventilation; PEEP = positive end expiratory pressure.

Evidences

- Prophylactic NIV
  - Post abdominal surgery
    - Post operative prophylactic CPAP has shown to improve oxygenation without any effect on reintubation rate.
    - Whereas post operative CPAP (via helmet) in selected group of patients (P/F<300 after 1hr post op) has shown to decrease reintubation rate and ICU length of stay significantly in comparison to standard oxygen therapy.

JAMA 293:589–595

- Post thoracic surgery
  - perioperative NIV in patients with FVC <70% has shown to decrease hospital length of stay significantly.

    Respir Med 101:1572–1578

- Post cardiac surgery
  - CPAP has shown to decrease pulmonary complications significantly after cardiac surgery
- Post bariatric surgery
  - Post operative CPAP has shown to faster recovery of lung volumes post surgery.

- Therapeutic NIV
  - Post abdominal surgery:
    - NIV (via helmet) for post abdominal surgery acute respiratory failure (defined as PaO2<60 and RR>25) has shown to decrease intubation rate, nosocomial pneumonia and other complication significantly without any effect on ICU mortality.

      Respir Care 52:1463–1471

  - Post thoracic surgery:
    - Usefulness of NIV post lung resection has been proven in an RCT (that has been discussed later)
  - Post cardiac surgery:
    - NPPV has been compared with CPAP in several RCT for post op atelectasis or respiratory failure without significant difference.

  - Post SOT
    - NPPV has shown in an RCT to significantly decrease intubation rate in post SOT respiratory failure paatients.

Clinical trial- NIV post lung resection

Method	Prospective RCT
Participants	48 patients who were admitted in ICU post lung resection with AHRI defined as RR>25, P/F<200, CXR abnormality were randomly assigned in 2 group
intervention	Intervention group received NPPV via cushion bridge nasal mask with target TV 8-10 ml/kg and respiratory rate <25/min
Comparator	Received oxygen via venturi mask
Outcome	Primary outcome was intubation rate Secondary outcome was in hospital and 120 day mortality, ICU and hospital length of stay etc.

TABLE 3. ENDOTRACHEAL MECHANICAL VENTILATION, MORTALITY, AND LENGTH OF INTENSIVE CARE UNIT AND HOSPITAL STAYS

	No-NPPV (*n* = 24) Mean ± SD	NPPV (*n* = 24) Mean ± SD	p Value*
ETMV, n (%)	12 (50%)	5 (20.8%)	0.035
In-hospital deaths, n (%)	9 (37.5%)	3 (12.5%)	0.045
Length of ICU stay, d	14 ± 11.1	16.65 ± 23.6	0.52
Length of hospital stay, d	22.8 ± 10.7	27.1 ± 19.5	0.61
120 - d mortality, n (%)	9 (37.5%)	3 (12.5%)	0.045

Definition of abbreviations: ETMV = endotracheal mechanical ventilation; ICU = intensive care unit; NPPV = noninvasive positive pressure ventilation

* p values are for the between-group comparisons for each variable.

Am J Respir Crit Care Med Vol 164. pp 1231–1235, 2001

Blunt trauma chest

- Recommendation
  - no recommendation about the use of noninvasive positive-pressure ventilation in patients who have chest trauma and respiratory distress, because of a lack of RCTs

CMAJ, February 22, 2011, 183(3)

RCT

chest -january 2010

Method	Single center prospective RCT
Participants	Patients >18 year of age who developed early hypoxemia (i.e. within 48 hours) after chest trauma. The study was stopped after inclusion of 25 patients due to efficacy.
Intervention	Bilevel ventilation via full face mask
Comparator	Standard oxygen therapy with epidural analgesia
Outcome	Primary end point was intubation rate Secondary end points were –pneumonia, pneumothorax, sepsis, ICU and hospital stay

Table 2—*Intubation and Secondary Outcome Variables of Patients*

	NIMV Group (n = 25)	Control Group (n = 25)	*P* Value
Intubation rate	3 (12%)	10 (40%)	.02
Causes of intubation			
Signs of exhaustion	2 (8%)	6 (24%)	.1
Refractory hypoxemia	0 (0%)	2 (8%)	
Inability to clear respiratory secretions	1 (4%)	1 (4%)	
Major agitation	0 (0%)	1 (4%)	
Pneumothorax post randomization	6 (24%)	3 (12%)	.3
Ventilator-associated pneumonia	2 (8%)	3 (12%)	.6
ARDS	3 (12%)	4 (16%)	.7
Sepsis	3 (12%)	2 (8%)	.6
Multiorgan failure	2 (8%)	1 (4%)	.8
ICU stay, d[a]	6 (5-10)	8 (6-13)	.4
ICU mortality	1 (4%)	1 (4%)	1.0
Hospital stay, d[a]	14 (10-17)	21 (17-29)	.001
Hospital mortality	1 (4%)	1 (4%)	1.0

See Table 1 for expansion of abbreviations.

[a]Expressed as median (25th-75th percentiles)

During bronchoscopy in AHRF

- Recommendation
  - no recommendation could be made about the use of either noninvasive positive-pressure ventilation or continuous positive airway pressure in patients who have hypoxemia and who undergo bronchoscopy, because of insufficient evidence

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Clinical trial

Massimo Antonelli, MD –chest 2002

Method	Prospective RCT
Participants	26 patients admitted in ICU with acute hypoxemic respiratory failure with suspected nosocomial pneumonia.
Intervention	NPPV was given from a ventilator through full face mask. FiO2 was kept at 90% during the procedure; EPAP was set at 5cm of H2O and IPAP 15-17 cm of H2O.
comparator	Standard oxygen therapy was given via a specially designed venturi mask to ensure FiO2 of 90% during procedure and allow entry of bronchoscope through a separate port
Outcome	Changes in P/F ratio during bronchoscopy, within 60minutes, hemodynamic instability and intubation rate within 24 hours

Table 1—*Baseline Characteristics of Patients and Outcome

Characteristics	Noninvasive ventilation (n = 13)	Standard treatment (n = 13)	p Value
Age, yr	52 ± 20	57 ± 15	0.5
Male gender	8 (61)	8 (61)	0.5
SAPS II	26 ± 11	27 ± 7	0.5
Underlying diagnosis			
COPD	5 (38)	2 (15)	0.18
Trauma	2 (15)	1 (7)	0.5
Pulmonary edema	2 (15)	2 (15)	0.7
Sepsis	2 (15)	2 (15)	0.7
Rhabdomyolysis	0	2 (15)	0.2
Sequential lung transplant	0	1 (7)	0.5
Cystic fibrosis	1 (7)	0	0.5
Severe acute hepatitis	1 (7)	0	0.5
Diabetic ketoacidosis	1 (7)	0	0.5
Pemphigus	0	1 (7)	0.5

*Values given as mean ± SD or No. (%), unless otherwise indicated.

Table 2—*Physiologic Variables and Outcomes of the Two Groups Before, During, and After Bronchoscopy**

Variable	NPPV Group (n = 13)	Standard Treatment Group (n = 13)	p Value
Baseline			
Respiratory rate, breaths/min	35 ± 4	36 ± 4	0.18
Pa_{O_2}/F_{IO_2} ratio	143 ± 32	155 ± 24	0.30
Pa_{CO_2}, mm Hg	50 ± 22	40 ± 8	0.15
pH	7.4 ± 0.07	7.4 ± 0.07	0.18
Heart rate, beats/min	94 ± 27	103 ± 20	0.35
MAP, mm Hg	88 ± 10	96 ± 13	0.08
During bronchoscopy			
Respiratory rate, breaths/min	31 ± 4	33 ± 4	0.12
Pa_{O_2}/F_{IO_2} ratio	261 ± 100	139 ± 38	< 0.001
Pa_{CO_2}, mm Hg	48 ± 17	39 ± 8	0.13
pH	7.41 ± 0.06	7.44 ± 0.08	0.26
Heart rate, beats/min	98 ± 22	104 ± 10	0.37
MAP, mm Hg	87 ± 7	81 ± 13	0.12
1 h after bronchoscopy			
Respiratory rate, breaths/min	29 ± 4	32 ± 4	0.20
Pa_{O_2}/F_{IO_2} ratio	176 ± 62	140 ± 38	0.09
Pa_{CO_2}, mm Hg	47 ± 15	39 ± 9	0.13
pH	7.41 ± 0.04	7.44 ± 0.08	0.31
Heart rate, beats/min	91 ± 18	108 ± 15	0.02
MAP, mm Hg	89 ± 7	78 ± 18	0.08
Outcome			
Patients requiring endotracheal intubation within 10 h of FOB	1 (7)	2 (15)	0.50
Mortality	4 (30)	7 (54)	0.16

*Values given as mean ± SD or No. (%), unless otherwise indicated.

NIV vs HFNC –

Simon et al. Critical Care (2014) 18:712

Method	Prospective RCT
Participants	40 critically ill patients admitted in medical/ surgical ICU with hypoxemia (P/F<300) who required diagnostic or therapeutic bronchoscopy were enrolled.
Intervention	Oxygenation via HFNC @ 50l/min o2 flow
Comparator	NIV through an ICU ventilator
Outcome	Primary outcome was lowest SpO2 recorded during FOB, Secondary outcomes were changes in blood gases upto 50 minutes, requirement of intubation within 8hrs or during ICU stay.

Table 1 Patient characteristics *(Continued)*

Physiological parameters at baseline			
Heart rate (beats/min)	95 ± 14	101 ± 15	0.27
Mean arterial pressure (mm Hg)	85 ± 11	82 ± 14	0.56
Respiratory rate (breaths/min)	30 ± 8	30 ± 9	0.86
PaO_2/FiO_2 (mm Hg)	163 ± 64	138 ± 69	0.25
$PaCO_2$ (mm Hg)	43 ± 13	34 ± 6	0.01
pH	7.43 ± 0.11	7.46 ± 0.07	0.21

Values are given as mean and standard deviation or as numbers and percentages. FiO_2, fraction of inspired oxygen; HFNC, high-flow nasal cannula; NIV, non-invasive ventilation; $PaCO_2$, partial pressure of carbon dioxide in arterial blood; PaO_2, partial pressure of oxygen in arterial blood; SAPS II, simplified acute physiology score II.

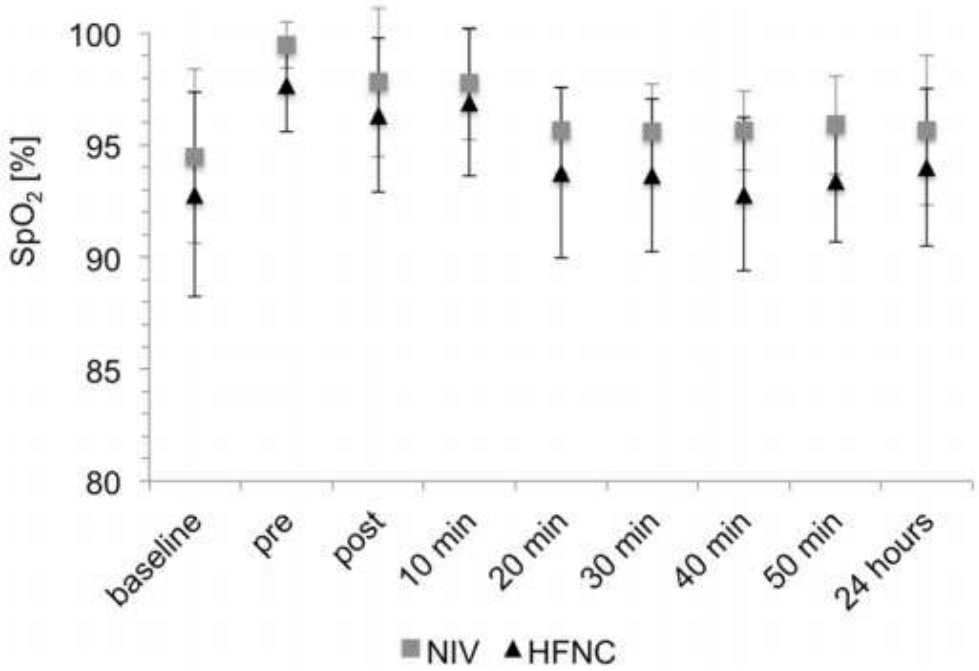


Figure 3 SpO_2 at baseline, pre and post bronchoscopy. Changes in SpO_2. Values are given as mean and standard deviation. HFNC, high-flow nasal cannula; NIV, non-invasive ventilation; SpO_2, oxygen saturation recorded by pulse oximetry.

For preoxygenation in patients with AHRF

Method	prospective RCT
Participants	53 patients admitted in 2 french ICU with AHRF requiring intubation
Intervention	After randomization patients assigned to NIV group received bilevel PAP via full face mask from a ICU ventilator for 3 minutes with FiO2 100%, PEEP 5 and target TV 7-10ml/kg
Comparator	In the oxygen group patient received 3 minutes of O2 via non rebreathing bag valve mask with occassional assistance at a flow rate of 15l/min
Outcome	Primary end point was drop in SpO2 during ETI

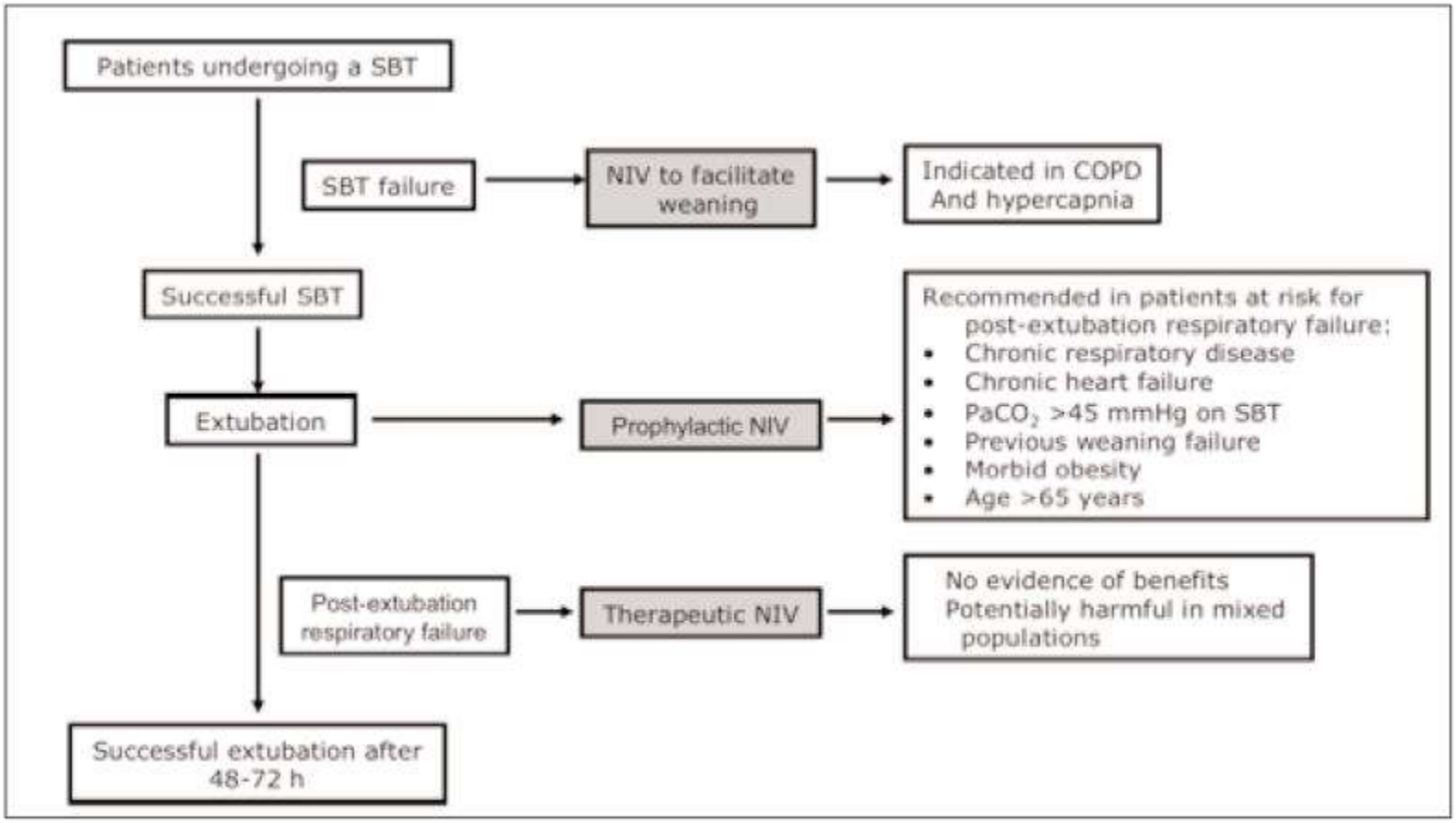
TABLE 4. ENDOTRACHEAL INTUBATION–RELATED COMPLICATIONS AND OUTCOME

	Control ($n = 26$)	NIV ($n = 27$)	p Value
$Sp_{O_2} < 80\%$	12 (46)	2 (7)	< 0.01
Regurgitation, n (%)	2 (8)	1 (4)	1
New infiltrate on post-ETI procedure chest X ray, n (%)	3 (12)	1 (4)	0.55
Duration of mechanical ventilation, d	10 (7–16)	9 (6–17)	0.89
ICU length of stay, d	17 (12–23)	18 (11–26)	0.92
ICU mortality, n	13 (50)	8 (30)	0.21

Definition of abbreviations: ETI = endotracheal intubation; ICU = intensive care unit; NIV = noninvasive ventilation.
The data are medians (interquartile range), or absolute numbers (%).
$p < 0.05$.

Am J Respir Crit Care Med Vol 174. pp 171–177, 2006

Post extubation respiratory failure



Preventive NIV -Recommendation

- The use of NIV routinely after extubation for reducing incidence of respiratory failure and reintubation rate is not recommended. (Level II).NIV can be recommended in patients after extubation who have a high risk of developing respiratory failure and reintubation (age>65 yrs, APACHE II>12 at the time of extubation, cardiac failure at the time of intubation). (Level I)

  Indian J Crit Care Med April-June 2006 Vol 10 Issue 2.

- We suggest that noninvasive positivepressure ventilation be used after planned extubation in patients who are considered to be at high risk of recurrent respiratory failure, but only in centres that have expertise in this type of therapy (grade 2B recommendation).

  CMAJ, February 22, 2011, 183(3).

Evidences

Noninvasive ventilation to prevent respiratory failure after extubation in high-risk patients*

Stefano Nava; Cesare Gregoretti; Francesco Fanfulla; Enzo Squadrone; Mario Grassi; Annalisa Carlucci; Fabio Beltrame; Paolo Navalesi

Crit Care Med 2005 Vol. 33, No. 11

Design	Multi –center RCT
Participant	97 consecutive patients with comparable baseline characteristic requiring >48 hrs of mechanical ventilation and considered at high risk of post extubation respiratory failure.
Intervention	After a successful weaning trial, the patients were randomized to receive NIV for >8 hrs a day in the first 48 hrs or SMT.
Outcome	Compared with SMT, NIV had a lower rate of intubation ($p<0.027$) –the primary outcome. The NIV also resulted in reduction in ICU mortality mediated by the reduction in reintubation

Table 1. Criteria for enrollment

Mechanical ventilation >48 hrs
Successful weaning trial
Plus one or more of the following high-risk scenarios for reintubation features:
1. More than one consecutive failure of weaning trial
2. Chronic heart failure
3. $Paco_2$ >45 mm Hg after extubation
4. More than one comorbidity (excluding chronic heart failure)
5. Weak cough defined as Airway Care Score (10) values ≥8 and <12
6. Upper airways stridor at extubation not requiring immediate reintubation

Characteristics	NIV (n = 48)	Standard Treatment (n = 49)	*p* Value
Age, yrs	56.0 ± 19.3	53.2 ± 19.5	.47
Gender, female/male	17/31	19/30	.65
SAPS II	31.4 ± 0.3	32.5 ± 2.6	.60
Reason for initiation of mechanical ventilation, n (%)			
Pneumonia	8 (17)	9 (18)	.87
ARDS	6 (13)	5 (10)	.76
Postsurgical respiratory failure	4 (8)	4 (8)	.81
Trauma	4 (8)	4 (8)	.81
CHF	4 (8)	6 (12)	.49
	NYHA II (2)	NYHA II (2)	
	NYHA III (1)	NYHA III (3)	
	NYHA IV (1)	NYHA IV (1)	
COPD exacerbation	17 (36)	15 (31)	.36
Neurosurgery	3 (6)	5 (11)	.44
Others	2 (4)	1 (2)	.55

Table 5. Risk difference of univariate and multivariate equations calculated with the generalized linear models

Response Variable Y	Predictor Variable X, n (%)		Risk Difference, %	95% CI	*p* Value
Univariate	NIV	No NIV	−16	(−2, −31)	.027
Reintubation	4/48 (8)	12/49 (24)			
	NIV	No NIV	−12	(−25, +0.7)	.064
ICU mortality	3/48 (6)	9/49 (18)			
	Reintubation	No reintubation	+60	(+36, +84)	<.001
ICU mortality	10/16 (63)	2/81 (3)			
Multivariate	NIV	No NIV	−16	(−2, −31)	.027
Reintubation	4/48 (8)	12/49 (24)			
	NIV	No NIV	−1	(−8, +6)	.845
ICU mortality	6/48 (12)	6/49 (13)			
	Reintubation	No reintubation	+60	(+37, +83)	<.001
ICU mortality	10/16 (62)	2/81 (3)			

Therapeutic NIV

- The use of NIV to reduce chances of reintubation in the event of postextubation respiratory failure in nonCOPD cases is not recommended.

  Indian J Crit Care Med April-June 2006 Vol 10 Issue 2

- We suggest that noninvasive positivepressure ventilation not be routinely used in patients who do not have COPD and who have postextubation respiratory failure (grade 2C recommendation).

  CMAJ, February 22, 2011, 183(3)

Evidences

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Noninvasive Positive-Pressure Ventilation for Respiratory Failure after Extubation

Andrés Esteban, M.D., Ph.D., Fernando Frutos-Vivar, M.D.,
Niall D. Ferguson, M.D., Yaseen Arabi, M.D.,
Carlos Apezteguía, M.D., Marco González, M.D., Scott K. Epstein, M.D.,
Nicholas S. Hill, M.D., Stefano Nava, M.D., Marco-Antonio Soares, M.D.,
Gabriel D'Empaire, M.D., Inmaculada Alía, M.D., and Antonio Anzueto, M.D.

N Engl J Med 2004;350:2452-60.

Method	Multi center prospective RCT
Participants	Patients in 37 centers in eight countries who were electively extubated after at least 48 hours of mechanical ventilation and who had respiratory failure (predefined criteria) within the subsequent 48 hours
Intervention	Patients who were eligible were randomly assigned to receive either NIV through a full face mask or SMT. Patients had to receive their assigned treatment for at least 1 hr
Comparator	Standard medical therapy with O2 supplementation
Outcome	The study was stopped after an interim analysis due to increased mortality rate in NIV treated group ($p = 0.048$). So the study stopped after recruiting 200 patients. Till then there was no difference in reintubation rate but patients in NIV group had a significant delay in reintubation.

Table 1. Baseline Characteristics of the Patients, According to Study Group.*

Characteristic	Non-invasive Ventilation (N=114)	Standard Medical Therapy (N=107)	P Value
Age — yr	61±17	58±19	0.25
Female sex — no. (%)	47 (41)	47 (44)	0.68
Simplified Acute Physiology Score II on admission†	37±13	36±10	0.77
Reason for initiation of mechanical ventilation			0.65
Acute respiratory failure — no. (%)			
Pneumonia	28 (25)	20 (19)	
Postoperative respiratory failure	20 (18)	23 (21)	
Sepsis	13 (11)	11 (10)	
Trauma	11 (10)	7 (7)	
Cardiac failure	8 (7)	12 (11)	
Acute respiratory distress syndrome	4 (4)	8 (7)	
Other	12 (11)	10 (9)	
Acute-on-chronic respiratory failure — no. (%)			
Chronic obstructive pulmonary disease	14 (12)	9 (8)	
Asthma	1 (1)	3 (3)	
Neuromuscular disease — no. (%)	3 (3)	4 (4)	

NIV in bronchial asthma

- Recommendation
  - NIV should not be used routinely in acute asthma. [C]

    Thorax 2002
  - No recommendation for NIV/CPAP for acute exacerbation of asthma

    CMAJ 2011
  - NIV is not recommended for routine use of asthma exacerbation. (Level III)
  - NIV may be tried in ICU in patients of acute severe asthma who fail to respond quickly to medical treatment and have no contraindication. (Level II)

    IJCCM 2006

Non-invasive positive pressure ventilation for treatment of respiratory failure due to severe acute exacerbations of asthma (Review)

Lim WJ, Mohammed Akram R, Carson KV, Mysore S, Labiszewski NA, Wedzicha JA, Rowe BH, Smith BJ

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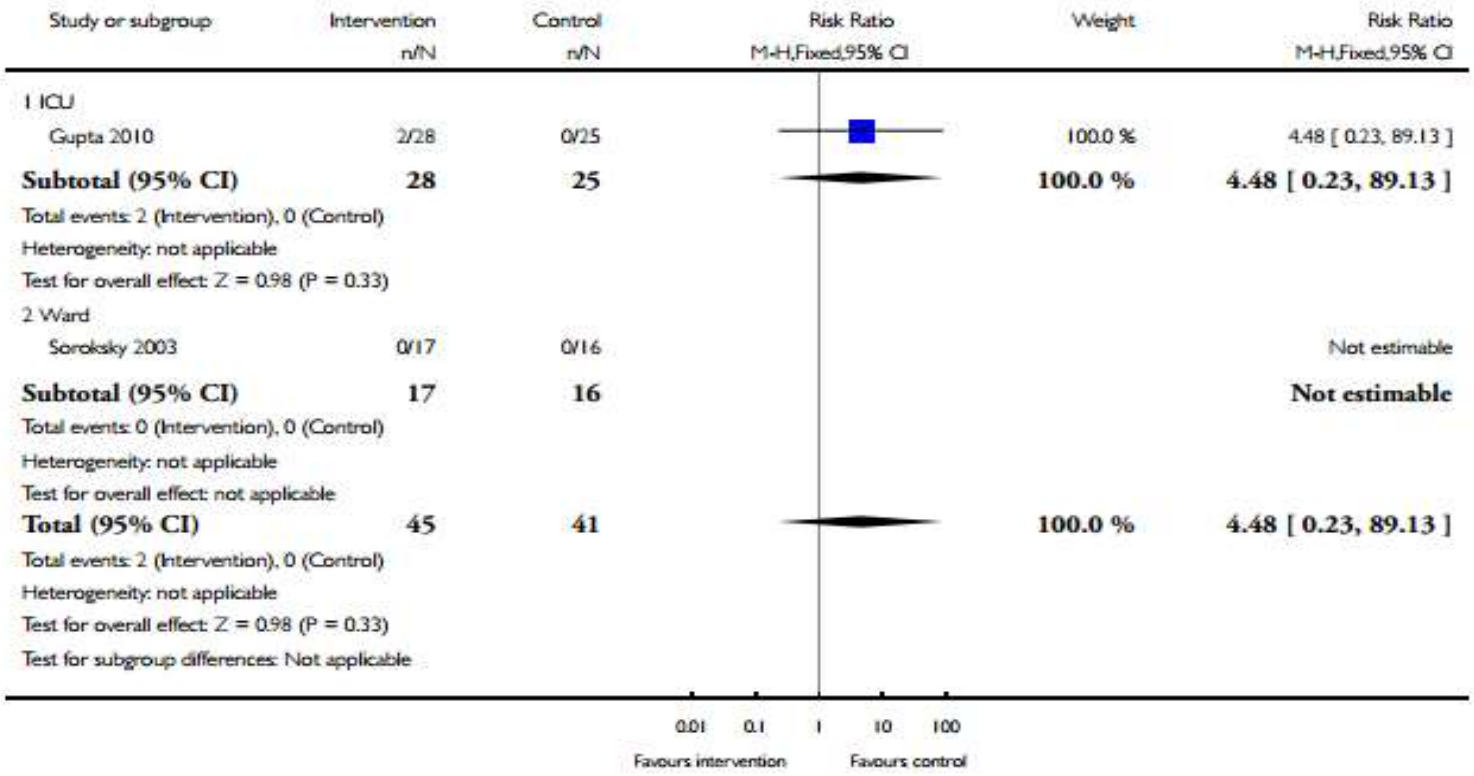
This is a reprint of a Cochrane review, prepared and maintained by The Cochrane Collaboration and published in *The Cochrane Library* 2012, Issue 12

Analysis 1.2. Comparison 1 NPPV versus usual care, Outcome 2 Endotracheal intubation.

Review: Non-invasive positive pressure ventilation for treatment of respiratory failure due to severe acute exacerbations of asthma

Comparison: 1 NPPV versus usual care

Outcome: 2 Endotracheal intubation

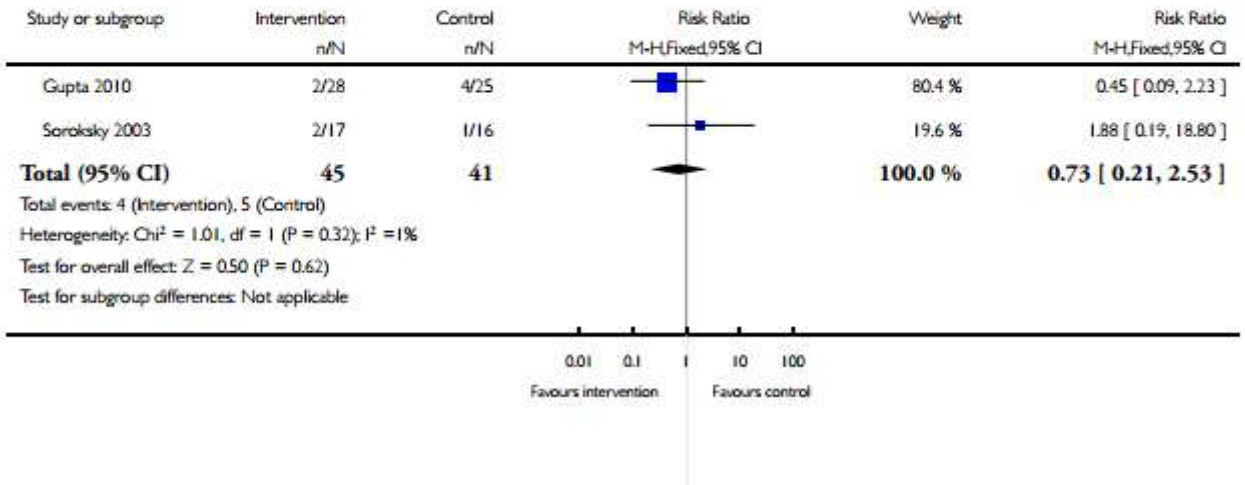


Analysis 1.5. Comparison 1 NPPV versus usual care, Outcome 5 Treatment failure.

Review: Non-invasive positive pressure ventilation for treatment of respiratory failure due to severe acute exacerbations of asthma

Comparison: 1 NPPV versus usual care

Outcome: 5 Treatment failure

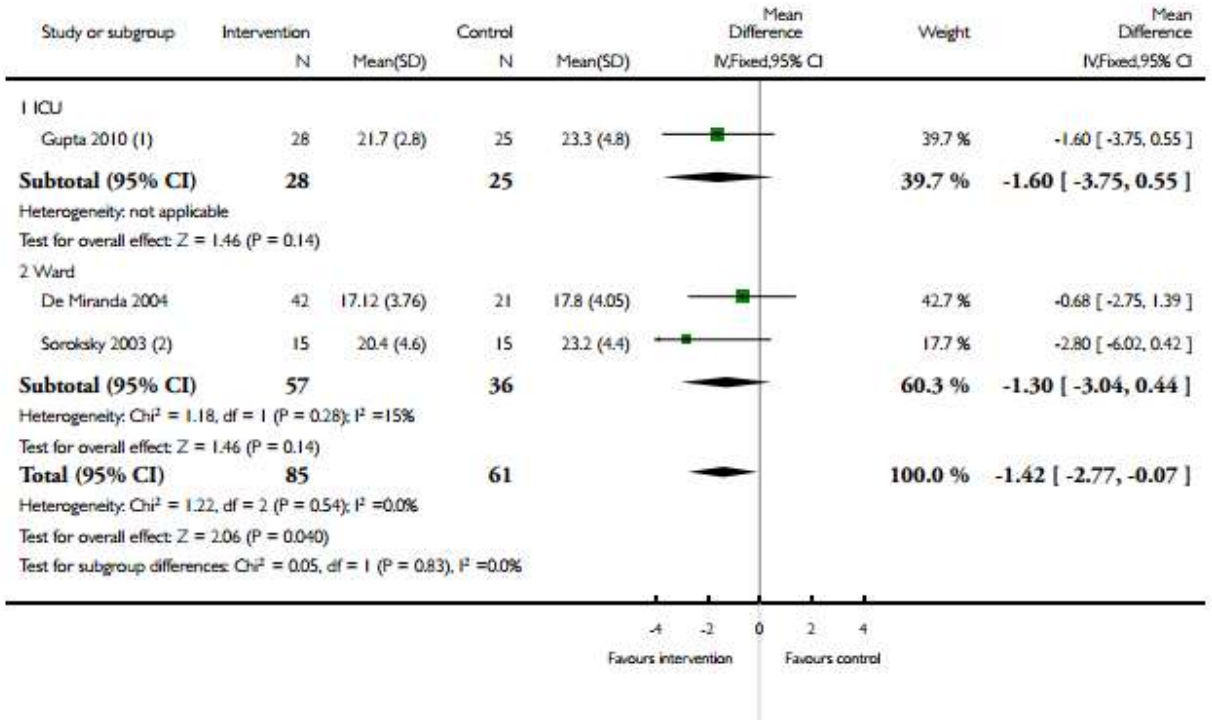


Analysis 1.15. Comparison 1 NPPV versus usual care, Outcome 15 Respiratory rate.

Review: Non-invasive positive pressure ventilation for treatment of respiratory failure due to severe acute exacerbations of asthma

Comparison: 1 NPPV versus usual care

Outcome: 15 Respiratory rate



Clinical trial

Method	Prospective RCT
Participants	53 patient with acute severe asthma who fulfill the eligibility criteria were randomized to receive either NPPV or standard medical therapy
Intervention	NPPV with standard medical therapy
Comparator	Standard medical therapy
Outcome	Primary outcome was improvement in lung function, hospital and ICU stay Secondary outcomes were time to resolution, bronchodilator use, failure of primary therapy.

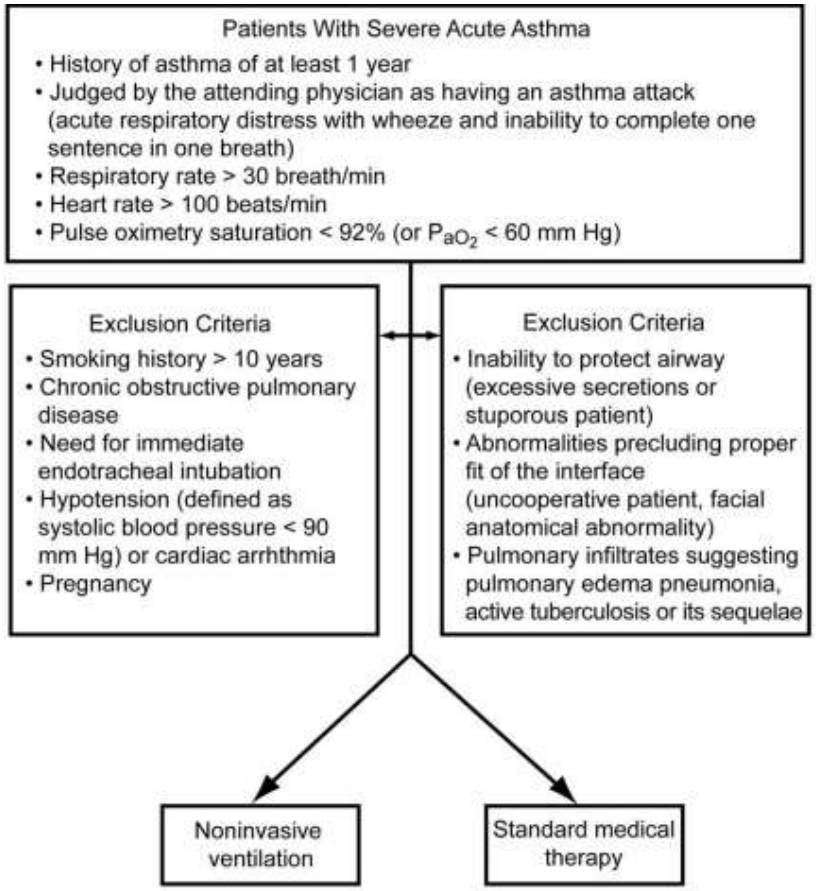


Fig. 1. Flowchart of inclusion and exclusion process.

Table 3. Outcomes

	Standard Medical Therapy (n = 25)	NIV (n = 28)	P
Primary Outcomes			
≥ 50% improvement in FEV_1 over baseline (n, %)			
At 1 h	11 (44)	10 (36)	.62
At 2 h	12 (48)	15 (54)	.70
At 4 h	16 (64)	24 (86)	.08
ICU stay (median and IQR h)	24 (18–36)	10 (8–20)	.01
Hospital stay (median and IQR h)	54 (48–72)	38 (24–48)	.01
Secondary Outcomes			
Time to disappearance of accessory muscle use (mean ± SD h)	3.2 ± 1.7	2.3 ± 1.4	.06
Dose of inhaled salbutamol (mean ± SD mg)	42.8 ± 10.4	31.2 ± 14.5	.008
Dose of inhaled ipratropium (mean ± SD mg)	7.6 ± 2.2	5.2 ± 2.8	.007
Failure of primary therapy (n, %)	4 (16)	2 (7)	.35

FEV_1 = forced expiratory volume in the first second
IQR = interquartile range

Trends in NIV use -15years registry

Table 1 Main patient characteristics and comparison of patients with noninvasive ventilation and invasive mechanical ventilation as the first-line ventilatory support modality

Characteristics, *N* (%) or median (IQR)	Study cohort *N* = 3,163	First-line NIV	First-line IMV	*P* value
Male gender	1,929 (61 %)	582 (60 %)	1,347 (62 %)	0.3
Age in years	66 (54–76)	69 (57–78)	64 (52–75)	<0.0001
Admitted from a hospital ward	1,162 (37 %)	367 (38 %)	795 (36 %)	0.5
Reason for admission				<0.0001
Shock	8,706 (28 %)	83 (9 %)	787 (36 %)	
ARF	1,208 (38 %)	538 (55 %)	670 (31 %)	
Acute-on-chronic respiratory failure	322 (10 %)	218 (22 %)	104 (5 %)	
Acute renal failure	99 (3 %)	30 (3 %)	69 (3 %)	
Coma	465 (15 %)	18 (2 %)	447 (20 %)	
Etiologies of ARF				
Pneumonia	692 (21.9)	221 (22.7)	471 (21.5)	0.5
COPD exacerbation	660 (20.9)	381 (39.1)	279 (12.7)	<0.0001
Chronic health status (McCabe)				<0.0001
No fatal disease	1,627 (51 %)	438 (45 %)	1,189 (54 %)	
Ultimately fatal disease	1,258 (40 %)	471 (48 %)	787 (36 %)	
Rapidly fatal disease	278 (9 %)	65 (7 %)	213 (10 %)	
SAPS II	47 (35–64)	35 (27–43)	55 (42–70)	<0.0001
SOFA day-1 coagulation subscore >0	844 (27 %)	182 (19 %)	662 (30 %)	<0.0001
SOFA day-1 cardiovascular subscore >1	1,262 (40 %)	114 (12 %)	1,148 (52 %)	<0.0001
SOFA day-1 neurologic subscore >0	1,492 (47 %)	215 (22 %)	1,277 (58 %)	<0.0001
SOFA day-1 hepatic subscore >0	592 (19 %)	118 (12 %)	474 (22 %)	<0.0001
SOFA day-1 renal subscore >1	1,033 (33 %)	238 (24 %)	795 (36 %)	<0.0001
Study group				<0.0001
Acute-on-chronic respiratory failure	1,036 (33 %)	543 (56 %)	493 (23 %)	
Cardiogenic pulmonary edema	1,156 (36 %)	258 (27 %)	898 (41 %)	
Immunocompetent	510 (16.1)	51 (5.2)	459 (21)	
Immunocompromised	461 (14.6)	122 (12.5)	339 (15.5)	
Nosocomial infection				
Nosocomial pneumonia	379 (12 %)	51 (5 %)	328 (15 %)	<0.0001
Catheter-related infection	225 (7 %)	34 (4 %)	191 (9 %)	<0.0001
Urinary tract infection	393 (12 %)	75 (8 %)	318 (15 %)	<0.0001
Bacteremia	585 (19 %)	97 (10 %)	488 (22 %)	<0.0001
Days spent in the ICU	7 (4–14)	6 (4–10)	8 (4–16)	<0.0001
ICU mortality	652 (21 %)	65 (7 %)	587 (27 %)	<0.0001
Days spent in the hospital	21 (10–40)	19 (12–34)	22 (9–43)	0.3
Hospital mortality	949 (30 %)	143 (15 %)	806 (37 %)	<0.0001

Data are number (percent), unless otherwise stated, and were obtained by univariate analysis (Wilcoxon test or χ^2 test, as appropriate). Center was also tested ($P = 0.0001$). The SOFA subscore cutoffs were the observed median values

ARF Acute respiratory failure, *COPD* chronic obstructive pulmonary disease, *IQR* interquartile range, *ICU* intensive care unit, *IMV* invasive mechanical ventilation, *SAPS II* Simplified Acute Physiologic Score II; *SOFA* sequential organ failure assessment

Table 3 Effect on mortality of noninvasive ventilation as first-line ventilatory support modality, as assessed using a marginal structural model

Population	Crude HR (95 % CI)	*P* value	Adjusted HR[a] (95 % CI)	*P* value
Study cohort (n = 3,163)	0.82 (0.75–0.89)	<0.0001	0.75 (0.68–0.83)	<0.0001
Acute-on-chronic respiratory failure (n = 1,036)	0.50 (0.40–0.62)	<0.0001	0.71 (0.57–0.90)	0.004
Cardiogenic pulmonary edema (n = 1,156)	0.87 (0.77–0.99)	0.044	0.85 (0.70–1.03)	0.10
De novo respiratory failure immunocompromised (n = 461)	0.80 (0.66–0.99)	0.036	0.89 (0.70–1.13)	0.35
De novo respiratory failure immunocompetent (n = 510)	0.98 (0.79–1.20)	0.81	1.18 (0.87–1.59)	0.30

HR Hazard ratio; *CI* confidence interval, *NIV* noninvasive mechanical ventilation, *SAPS II* Simplified Acute Physiology Score II

[a] Adjustment for center, gender, reason for admission, chronic diseases, SAPS II, and chronic health status (McCabe) and duration of hospital stay before ICU admission

Intensive Care Med (2014) 40:582–591
DOI 10.1007/s00134-014-3222-y

Survey from INDIA

Table 1. Etiology of Acute Respiratory Failure Requiring 101 Applications of NIV in the Respiratory ICU

Etiology	no. (%)
Type 1 Respiratory Failure	
ALI/ARDS	12 (28.6)
Pneumonia	11 (26.2)
Interstitial lung diseases	9 (21.4)
Bronchial asthma	4 (9.5)
Others*	6 (14.3)
Type 2 Respiratory Failure	
COPD	17 (28.8)
Preemptive therapy of post-extubation respiratory failure	12 (20.3)
Bronchial asthma	9 (15.3)
Post-extubation respiratory failure	8 (13.6)
Allergic bronchopulmonary aspergillosis	7 (11.8)
Myasthenic crisis	3 (5.1)
Others†	3 (5.1)

* Diffuse alveolar hemorrhage, pulmonary embolism, pulmonary edema.
† Obstructive sleep apnea hypopnea syndrome, pulmonary edema
NIV = noninvasive ventilation
ALI = acute lung injury

Table 4. Outcome of NIV in Terms of Requirement for Endotracheal Intubation Among the Various Groups of Acute Respiratory Failure

Etiology	Success, no. (%)	Failure, no. (%)
Type 1 Respiratory Failure		
ALI/ARDS	3 (25)	9 (75)
Pneumonia	4 (36.4)	7 (63.6)
Interstitial lung diseases	1 (11.1)	8 (88.9)
Bronchial asthma	4 (100)	
Others*	2 (33.3)	4 (66.7)
Type 2 Respiratory Failure		
COPD	10 (58.8)	7 (41.2)
Preemptive therapy of post-extubation respiratory failure	12 (100)	
Bronchial asthma	3 (33.3)	6 (66.7)
Post-extubation respiratory failure		8 (100)
Allergic bronchopulmonary aspergillosis	4 (57.1)	3 (42.9)
Myasthenic crisis	2 (66.7)	1 (33.3)
Others†	3 (100)	

* Diffuse alveolar hemorrhage, pulmonary embolism, pulmonary edema.
† Obstructive sleep apnea hypopnea syndrome, pulmonary edema
NIV = noninvasive ventilation
ALI = acute lung injury

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Different modes on NIV

Table 6.1 Estimated percentage use of different modes of NIV during acute respiratory failure

• Pressure support	54 %
• Pressure controlled	14 %
• Volume assisted	4 %
• Proportional assisted	3 %
• CPAP	23 %
• Others	2 %

Site of care

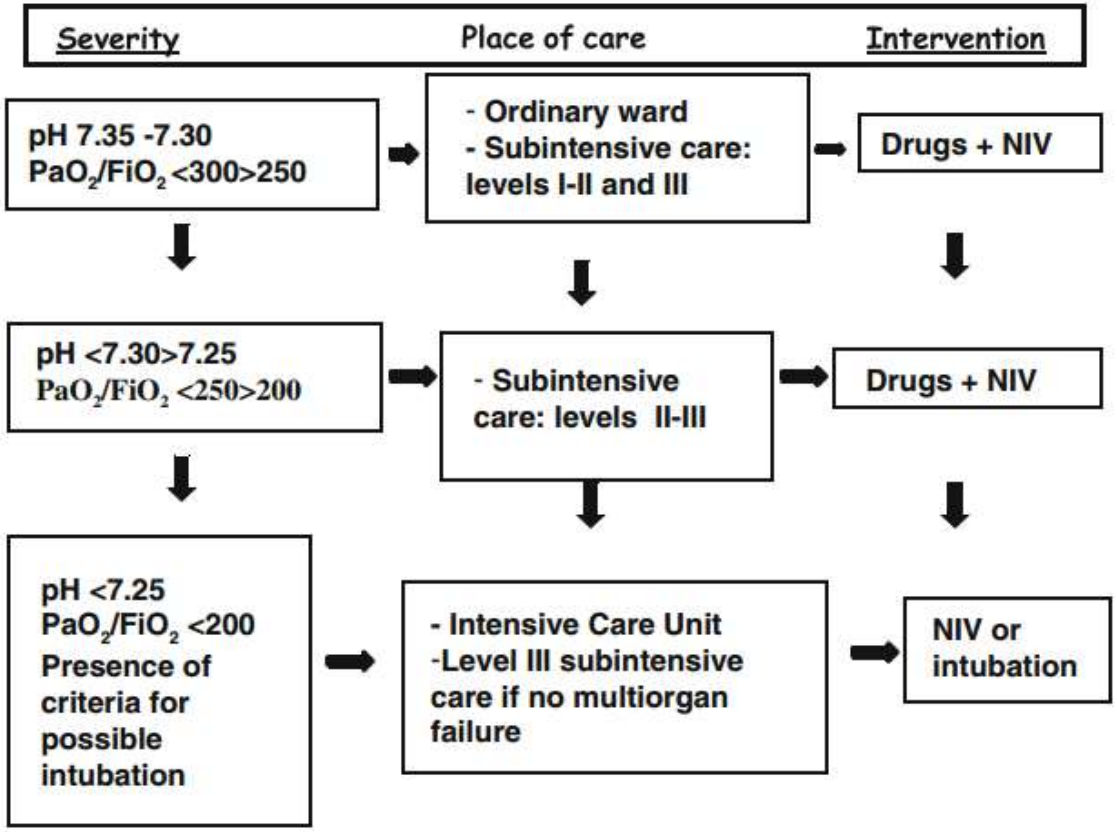
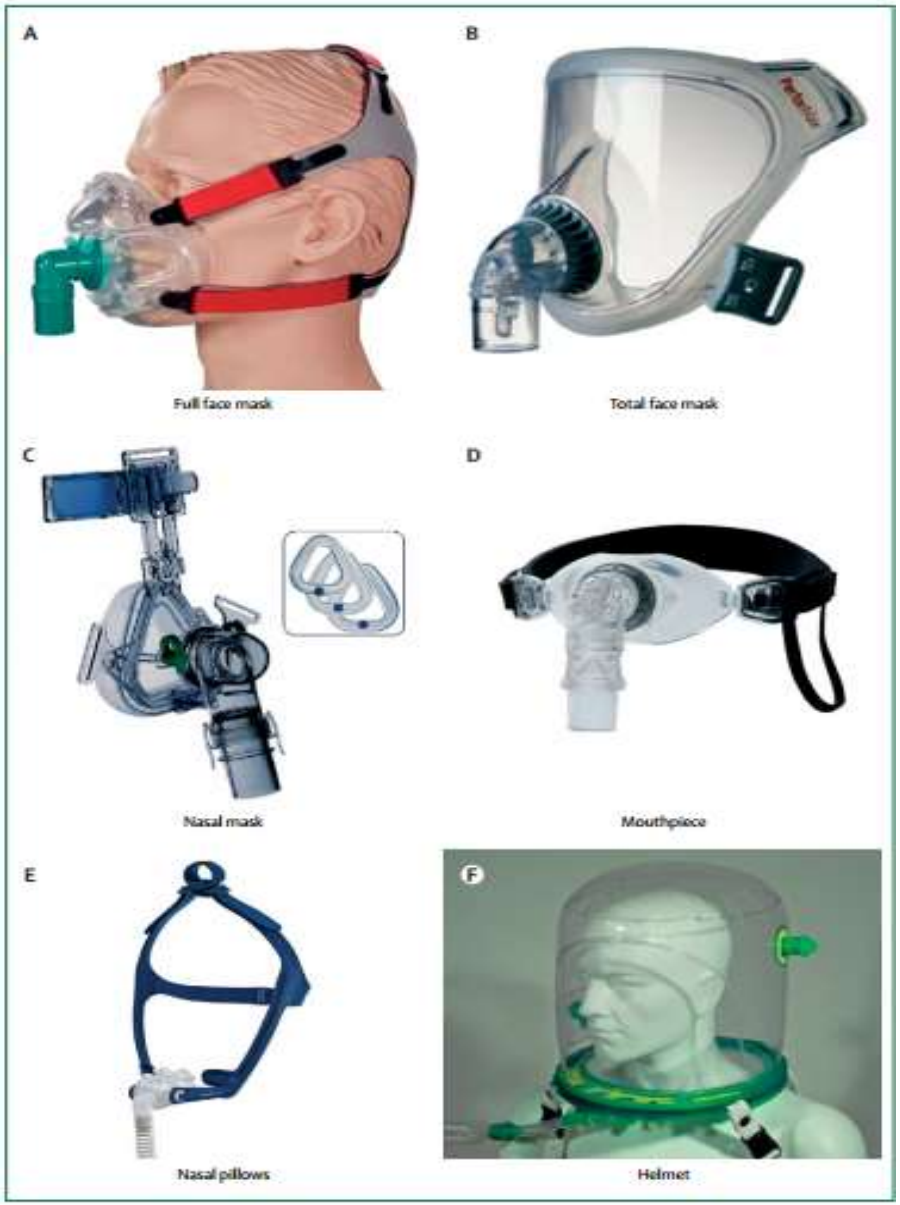


Fig. 17.1 Flow-chart of the use of NIV in hospital

S. Nava and F. Fanfulla, *Non Invasive Artificial Ventilation*,
DOI: 10.1007/978-88-470-5526-1_17, © Springer-Verlag Italia 2014

Different interfaces



Take home message

- NIV ***may*** be used as an adjunct to oxygen therapy in AHRF of different etiology to avoid intubation and related complications
- New and well designed RCT is required to confirm its role in clinical situations like early ARDS, severe pneumonia etc.