2019台灣胸腔暨重症加護醫學會夏季會

2019 Summer Workshop of Taiwan Society of Pulmonary and Critical Care Medicine

Updated guidelines for noninvasive ventilation

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Outline

- **Strong recommendation**

  -Hypercapnia with COPD exacerbation

  -Cardiogenic pulmonary edema

- **Conditional recommendation**

  -Immunocompromised

  -Post-operative

  -Palliative care

  -Trauma

  -Weaning in hypercapnic patients

  -Post-extubation in high risk patient

- **No recommendation**

  -*De novo* respiratory failure

Official ERS/ATS clinical practice guidelines: noninvasive ventilation for acute respiratory failure

Bram Rochwerg[1], Laurent Brochard[2,3], Mark W. Elliott[4], Dean Hess[5], Nicholas S. Hill[6], Stefano Nava[7] and Paolo Navalesi[8] (members of the steering committee); Massimo Antonelli[9], Jan Brozek[1], Giorgio Conti[9], Miquel Ferrer[10], Kalpalatha Guntupalli[11], Samir Jaber[12], Sean Keenan[13,14], Jordi Mancebo[15], Sangeeta Mehta[16] and Suhail Raoof[17,18] (members of the task force)

TABLE 1 Interpretation of strong and conditional recommendations for stakeholders (patients, clinicians and healthcare policy makers)

	Strong recommendation	Weak recommendation
For patients	Most individuals in this situation would want the recommended course of action and only a small proportion would not.	The majority of individuals in this situation would want the suggested course of action, but many would not.
For clinicians	Most individuals should receive the recommended course of action. Adherence to this recommendation according to the guideline could be used as a quality criterion or performance indicator. Formal decision aids are not likely to be needed to help individuals make decisions consistent with their values and preferences.	Different choices are likely to be appropriate for different patients and therapy should be tailored to the individual patient's circumstances. Those circumstances may include the patient or family's values and preferences.
For policy makers	The recommendation can be adapted as policy in most situations including for the use as performance indicators.	Policy making will require substantial debates and involvement of many stakeholders. Policies are also more likely to vary between regions. Performance indicators would have to focus on the fact that adequate deliberation about the management options has taken place.

Conditional Recommendation

Table 4. Paradigmatic situations in which a strong recommendation may be warranted despite low or very low confidence in effect estimates

Situation	Condition	Example
1	When low quality evidence suggests benefit in a life-threatening situation (evidence regarding harms can be low or high)	Fresh frozen plasma or vitamin K in a patient receiving warfarin with elevated INR and an intracranial bleed. Only low quality evidence supports the benefits of limiting the extent of the bleeding
2	When low quality evidence suggests benefit and high quality evidence suggests harm or a very high cost	Head-to-toe CT/MRI screening for cancer. Low quality evidence of benefit of early detection but high quality evidence of possible harm and/or high cost (strong recommendation against this strategy)
3	When low quality evidence suggests equivalence of two alternatives, but high quality evidence of less harm for one of the competing alternatives	*Helicobacter pylori* eradication in patients with early stage gastric MALT lymphoma with *H. pylori* positive. Low quality evidence suggests that initial *H. pylori* eradication results in similar rates of complete response in comparison with the alternatives of radiation therapy or gastrectomy; high quality evidence suggests less harm/morbidity
4	When high quality evidence suggests equivalence of two alternatives and low quality evidence suggests harm in one alternative	Hypertension in women planning conception and in pregnancy. Strong recommendations for labetalol and nifedipine and strong recommendations against angiotensin converting enzyme (ACE) inhibitors and angiotensin receptor blockers (ARB)—all agents have high quality evidence of equivalent beneficial outcomes, with low quality evidence for greater adverse effects with ACE inhibitors and ARBs
5	When high quality evidence suggests modest benefits and low/very low quality evidence suggests possibility of catastrophic harm	Testosterone in males with or at risk of prostate cancer. High quality evidence for moderate benefits of testosterone treatment in men with symptomatic androgen deficiency to improve bone mineral density and muscle strength. Low quality evidence for harm in patients with or at risk of prostate cancer

Abbreviations: INR, international normalized ratio; CT, computed tomography; MRI, magnetic resonance imaging; MALT, mucosa-associated lymphoid tissue.

Journal of Clinical Epidemiology 2013; 66:726-735.

Strength of Recommendations Grading System

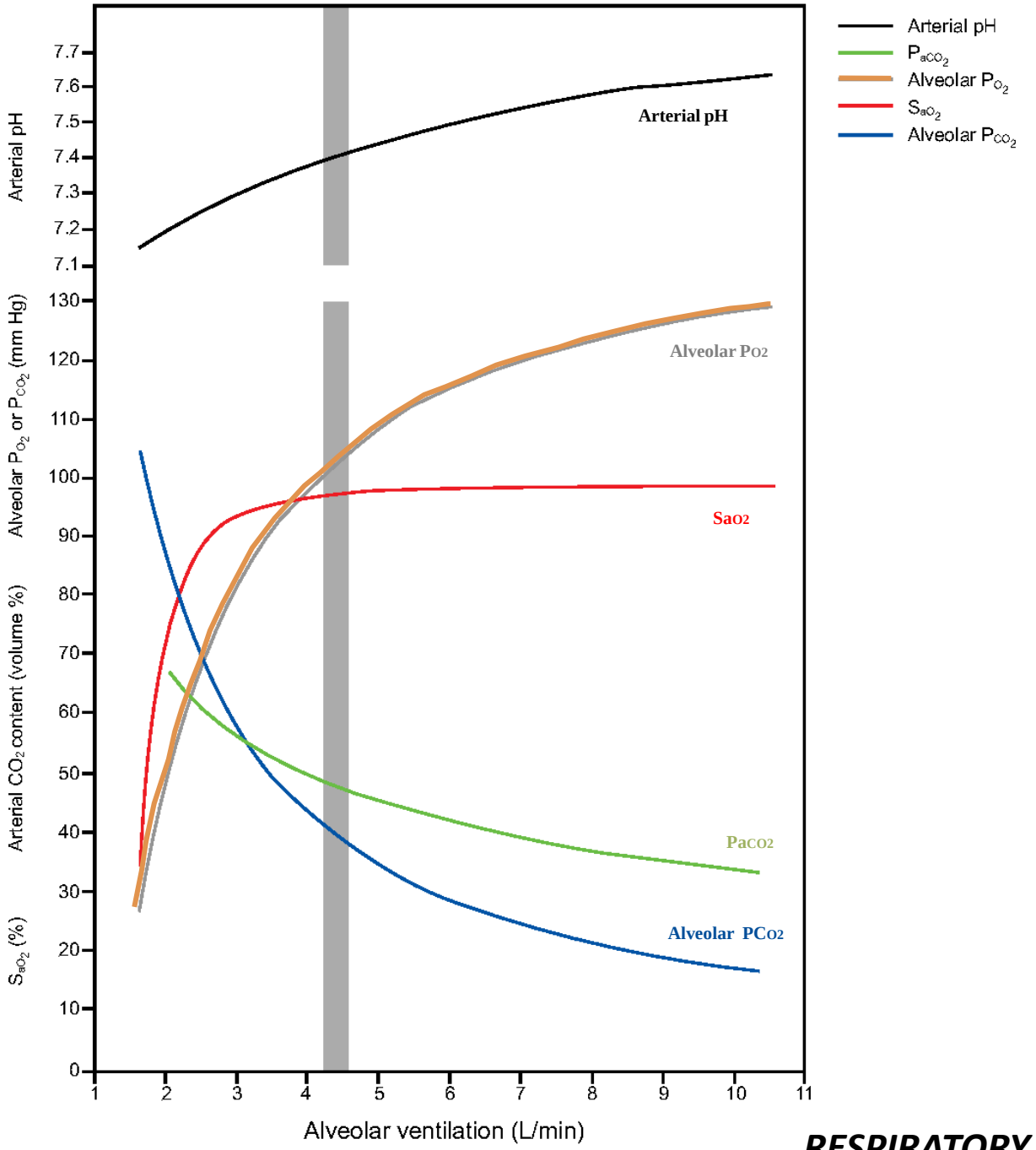
Grade of Recommendation	Benefit vs Risk and Burdens	Methodologic Strength of Supporting Evidence	Implications
Strong recommendation, high-quality evidence (1A)	Benefits clearly outweigh risk and burdens or vice versa.	Consistent evidence from randomized controlled trials without important limitations or exceptionally strong evidence from observational studies.	Recommendation can apply to most patients in most circumstances. Further research is very unlikely to change our confidence in the estimate of effect.
Strong recommendation, moderate-quality evidence (1B)	Benefits clearly outweigh risk and burdens or vice versa.	Evidence from randomized controlled trials with important limitations (inconsistent results, methodologic flaws, indirect or imprecise) or very strong evidence from observational studies.	Recommendation can apply to most patients in most circumstances. Higher-quality research may well have an important impact on our confidence in the estimate of effect and may change the estimate.
Strong recommendation, low- or very-low-quality evidence (1C)	Benefits clearly outweigh risk and burdens or vice versa.	Evidence for at least one critical outcome from observational studies, case series, or randomized controlled trials, with serious flaws or indirect evidence.	Recommendation can apply to most patients in many circumstances. Higher-quality research is likely to have an important impact on our confidence in the estimate of effect and may well change the estimate.
Weak recommendation, high-quality evidence (2A)	Benefits closely balanced with risks and burden.	Consistent evidence from randomized controlled trials without important limitations or exceptionally strong evidence from observational studies.	The best action may differ depending on circumstances or patient or societal values. Further research is very unlikely to change our confidence in the estimate of effect.
Weak recommendation, moderate-quality evidence (2B)	Benefits closely balanced with risks and burden.	Evidence from randomized controlled trials with important limitations (inconsistent results, methodologic flaws, indirect or imprecise) or very strong evidence from observational studies.	Best action may differ depending on circumstances or patient or societal values. Higher-quality research may well have an important impact on our confidence in the estimate of effect and may change the estimate.
Weak recommendation, low- or very-low-quality evidence (2C)	Uncertainty in the estimates of benefits, risks, and burden; benefits, risk, and burden may be closely balanced.	Evidence for at least one critical outcome from observational studies, case series, or randomized controlled trials, with serious flaws or indirect evidence.	Other alternatives may be equally reasonable. Higher-quality research is likely to have an important impact on our confidence in the estimate of effect and may well change the estimate.

Chest 2012; 141:53S-70S.

Quality Assessment Criteria.

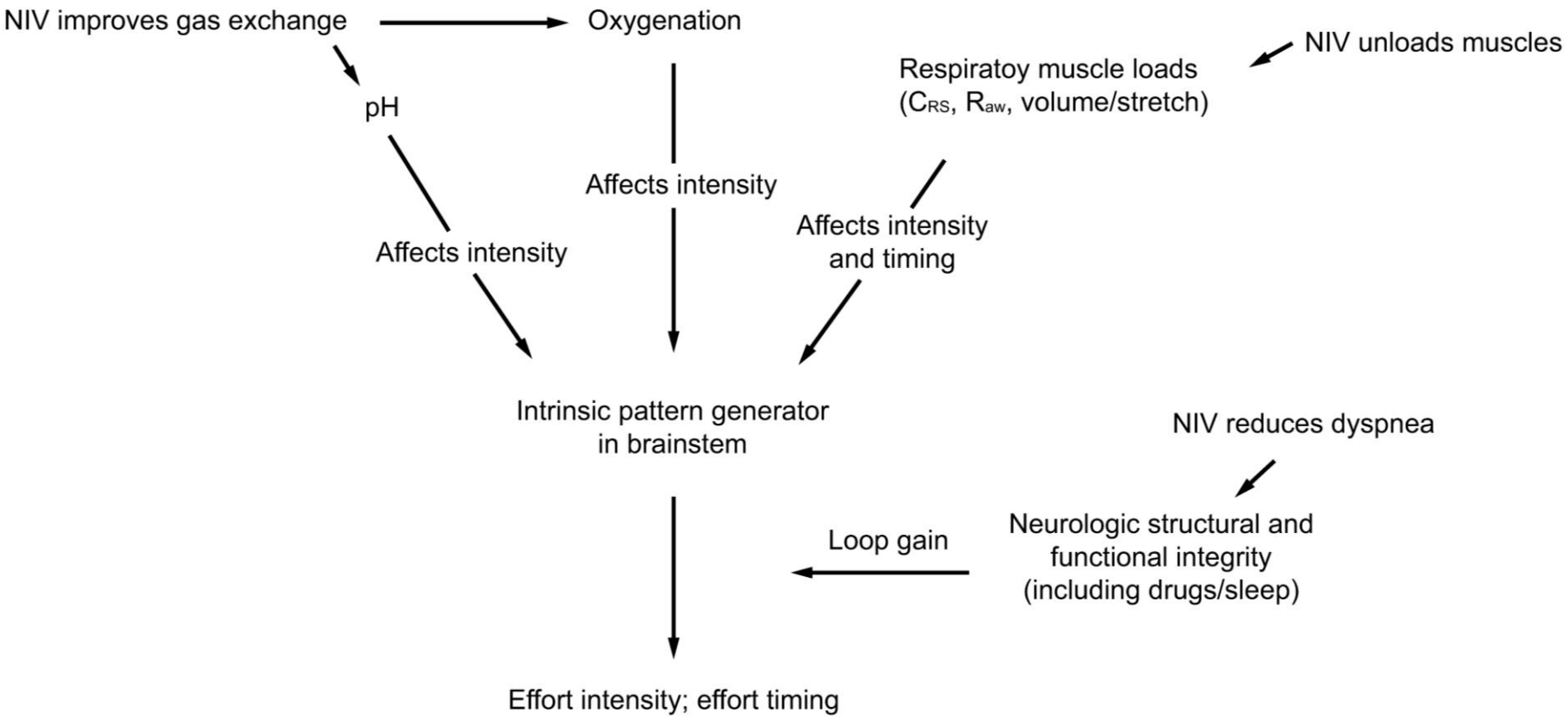
Study Design	Quality of Evidence	Lower if	Higher if
Randomized trial →	High	Risk of bias -1 Serious -2 Very serious	Large effect +1 Large +2 Very large
	Moderate	Inconsistency -1 Serious -2 Very serious	Dose response +1 Evidence of a gradient
Observational study →	Low	Indirectness -1 Serious -2 Very serious	All plausible confounding +1 Would reduce a demonstrated effect or
	Very low	Imprecision -1 Serious -2 Very serious	+1 Would suggest a spurious effect when results show no effect
		Publication bias -1 Likely -2 Very likely	

Journal of Clinical Epidemiology 2011; 64:383-394.



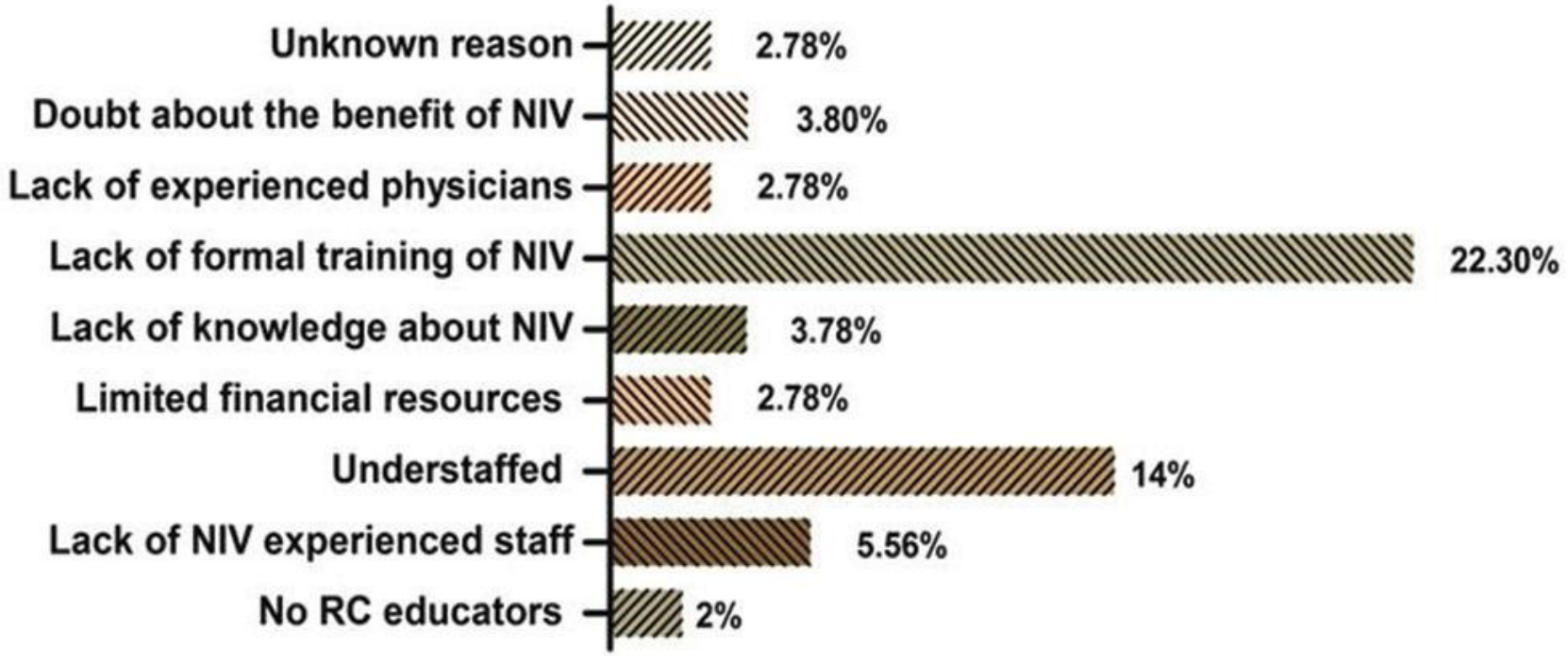
RESPIRATORY CARE 2019; 64:617-628.

NIV Effect on Ventilatory Control Center



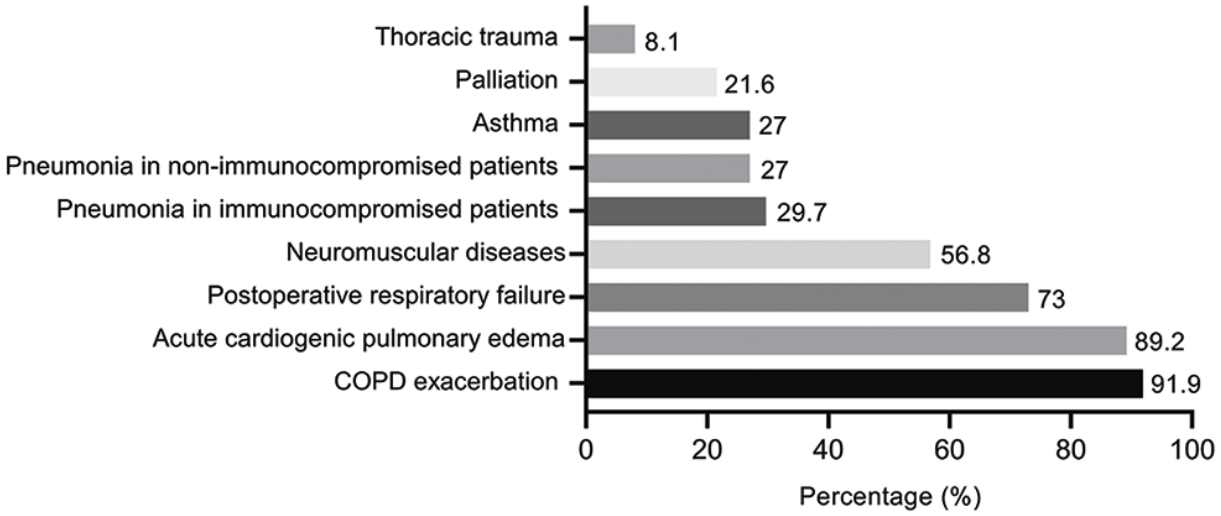
RESPIRATORY CARE 2019; 64:617-628.

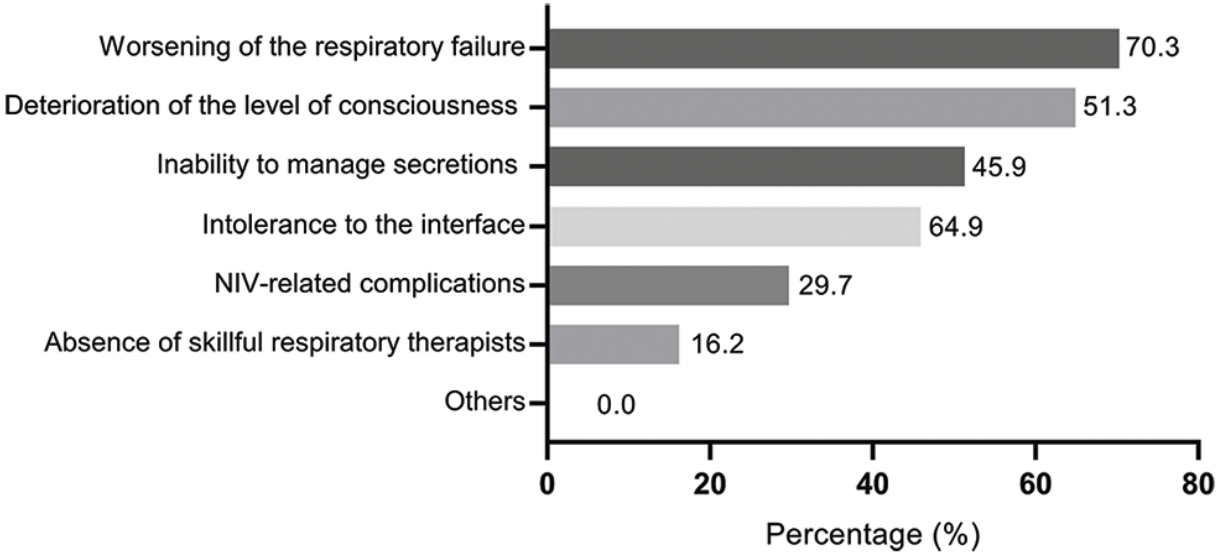
Underutilization of NIV



Annals of Thoracic Medicine 2018; 13:237-242.

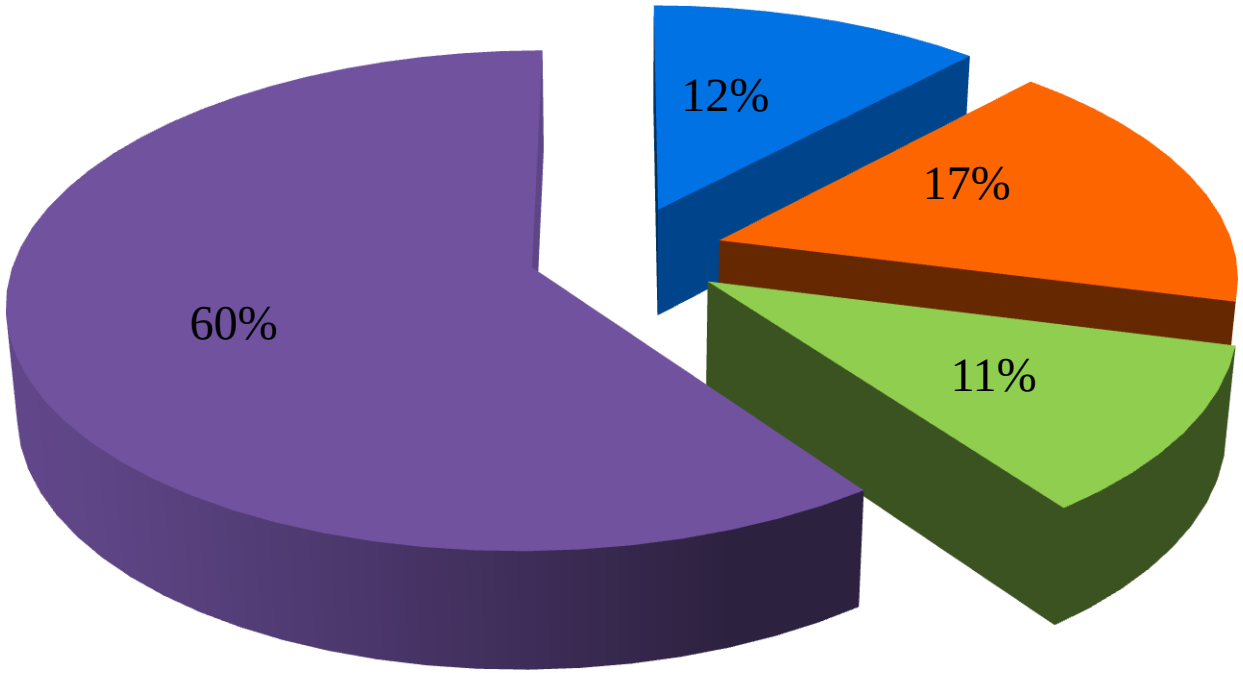
Indications and Failures of NIV





Annals of Thoracic Medicine 2018; 13:237-242.

Respondents' Confidence Rate of NIV



Annals of Thoracic Medicine 2018; 13:237-242.

TABLE 2 Recommendations for actionable PICO questions

Clinical indication[#]	Certainty of evidence[¶]	Recommendation
Prevention of hypercapnia in COPD exacerbation	⊕⊕	Conditional recommendation against
Hypercapnia with COPD exacerbation	⊕⊕⊕⊕	Strong recommendation for
Cardiogenic pulmonary oedema	⊕⊕⊕	Strong recommendation for
Acute asthma exacerbation		No recommendation made
Immunocompromised	⊕⊕⊕	Conditional recommendation for
***De novo* respiratory failure**		No recommendation made
Post-operative patients	⊕⊕⊕	Conditional recommendation for
Palliative care	⊕⊕⊕	Conditional recommendation for
Trauma	⊕⊕⊕	Conditional recommendation for
Pandemic viral illness		No recommendation made
Post-extubation in high-risk patients (prophylaxis)	⊕⊕	Conditional recommendation for
Post-extubation respiratory failure	⊕⊕	Conditional recommendation against
Weaning in hypercapnic patients	⊕⊕⊕	Conditional recommendation for

[#]: all in the setting of acute respiratory failure; [¶]: certainty of effect estimates: ⊕⊕⊕⊕, high; ⊕⊕⊕, moderate; ⊕⊕, low; ⊕, very low.

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Hypercapnia with COPD exacerbation

COPD with hypercapnia

PH>7.35
- Condition against

PH:7.25-7.35
- Strong recommend

PH<7.25
- Strong recommend

COPD post-extubation

Weaning
- Condition recommend

Prevention
- Condition recommend

Failure treat
- Condition against

Recommendation

- **We suggest NIV not be used in patients with hypercapnia who are not acidotic in the setting of a COPD exacerbation.**
- **(Conditional recommendation, low certainty of evidence)**

Bilevel NIV to prevent intubation

- **improvement in pH or respiratory rate, is a good predictor of a successful outcome**
- **response is almost universally seen within the first 1–4 h after NIV**
- **↓ dyspnoea**
- **↓ intubation rate**
- **↓ ICU admission**
- **↓ hospital length of stay**
- **↓ respiratory and nonrespiratory infection**
- **↑ survival**

Recommendations

- **We recommend bilevel NIV for patients with ARF leading to acute or acute-on-chronic respiratory acidosis (pH ⩽7.35) due to COPD exacerbation.**
- **(Strong recommendation, high certainty of evidence.)**

Recommendations

- **We recommend a trial of bilevel NIV in patients considered to require endotracheal intubation and mechanical ventilation, unless the patient is immediately deteriorating.**
- **(Strong recommendation, moderate certainty of evidence.)**

Implementation considerations

- **Bilevel NIV should be considered when the pH is ⩽7.35, PaCO2 is >45 mmHg and the respiratory rate is >20–24 breaths/min despite standard medical therapy.**

- **Bilevel NIV remains the preferred choice for patients with COPD who develop acute respiratory acidosis during hospital admission.**
- **There is no lower limit of pH below which a trial of NIV is inappropriate**
- **However, the lower the pH, the greater risk of failure, and patients must be very closely monitored with rapid access to endotracheal intubation and invasive ventilation if not improving.**

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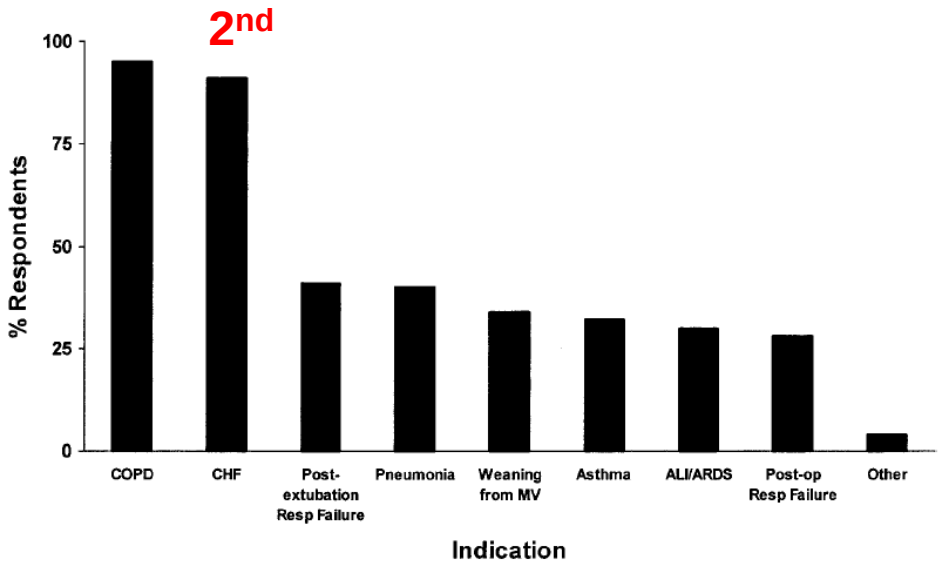
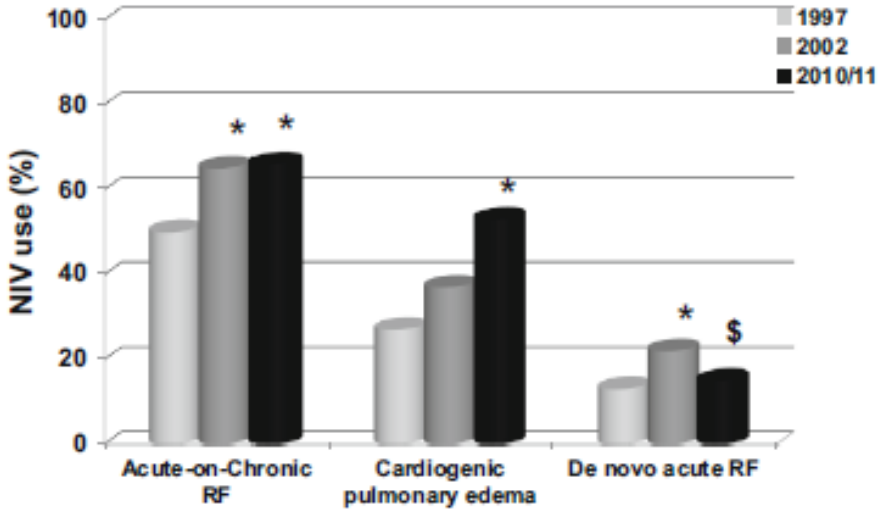
NIV in cardiogenic pulmonary edema

The increasing use of NIV in cardiogenic pulmonary edema (CPE)





CHF is the **2nd** most popular indication

The use of NIV in CPE is still increasing

Eur Heart J. 2018 Jan 1;39(1):17-25
Crit Care Med 2005;33:1477–83

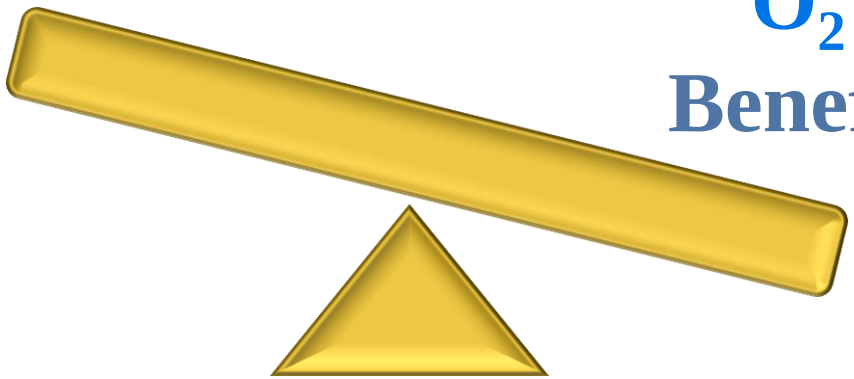
Physiological effect of PEEP

Table 2 **Main physiologic effects of positive intrathoracic pressure**

Cardiovascular
↓ Venous return → ↓ RV preload → ↓ LV preload
↑ Pulmonary vascular resistance → ↑ RV afterload → RV enlargement →↓ LV Compliance
↓ LV afterload (↓ systolic wall stress)
↓ Systemic blood pressure → ↓ Cardiac output[a]
Respiratory
Recruitment of collapsed alveoli → ↑Functional residual capacity
Maintenance continuously opened alveoli→ Gas exchange during the whole respiratory cycle
Intra-alveolar pressure against oedema
↓ Work of breathing
↑ Oxygenation

BP drop

Risk



O_2

Benefit

Eur Heart J. 2018 Jan 1;39(1):17-25

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Noninvasive Ventilation in Acute Cardiogenic Pulmonary Edema

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

CPAP or NIPPV was associated with greater reductions in **dyspnea**, **HR**, **acidosis** and **hypercapnia**

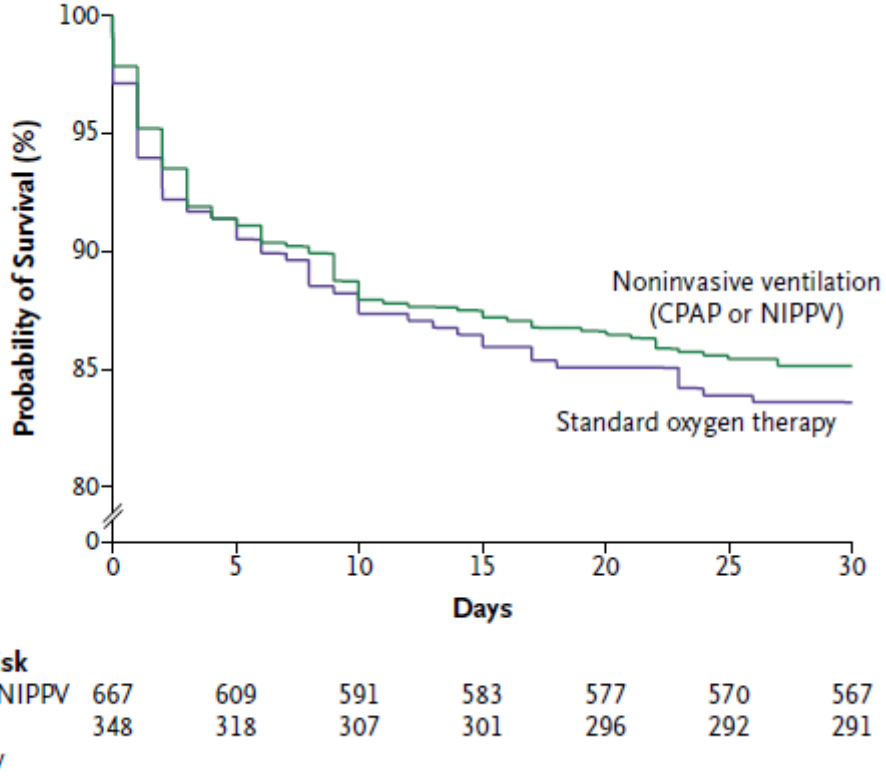
N Engl J Med 2008;359:142-51

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Noninvasive Ventilation in Acute Cardiogenic Pulmonary Edema

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



No outcome effect:

1. 7-d or 30-d death
2. Risk of intubation
3. ICU admission
4. Myocardial infarction risk

N Engl J Med 2008;359:142-51

Similar results of other studies

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

Lancet

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

Summary

Background Non-invasive positive pressure ventilation (NIPPV), using continuous positive airway pressure (CPAP) Lancet 2006; 367: 1155–63

Noninvasive Ventilation in Cardiogenic Pulmonary Edema

A Multicenter Randomized Trial

AJRCC

Stefano Nava, Giorgio Carbone, Nicola DiBattista, Andrea Bellone, Paola Baiardi, Roberto Cosentini, Mauro Marenco, Fabrizio Giostra, Guido Borasi, and Paolo Groff

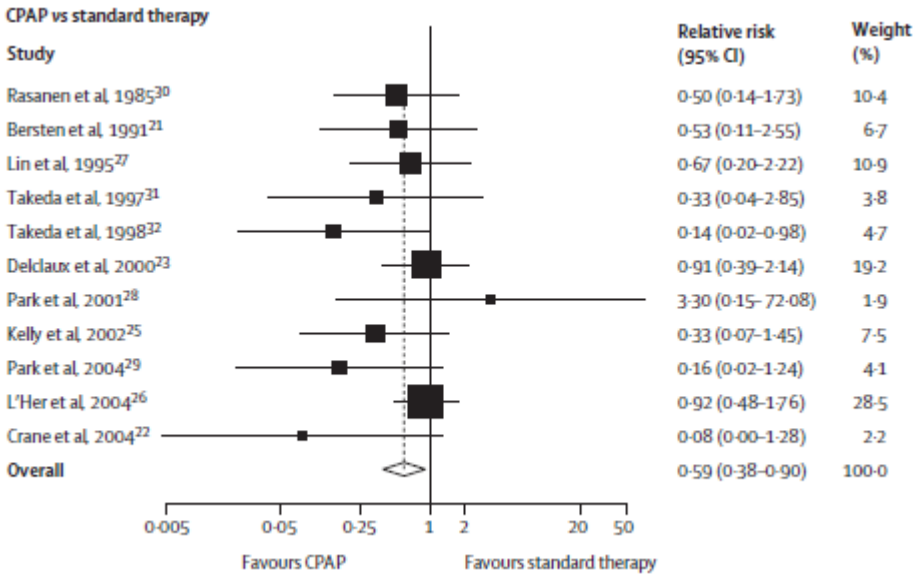
Circulation Journal
Official Journal of the Japanese Circulation Society
http://www.j-circ.or.jp

ORIGINAL ARTICLE
Critical Care

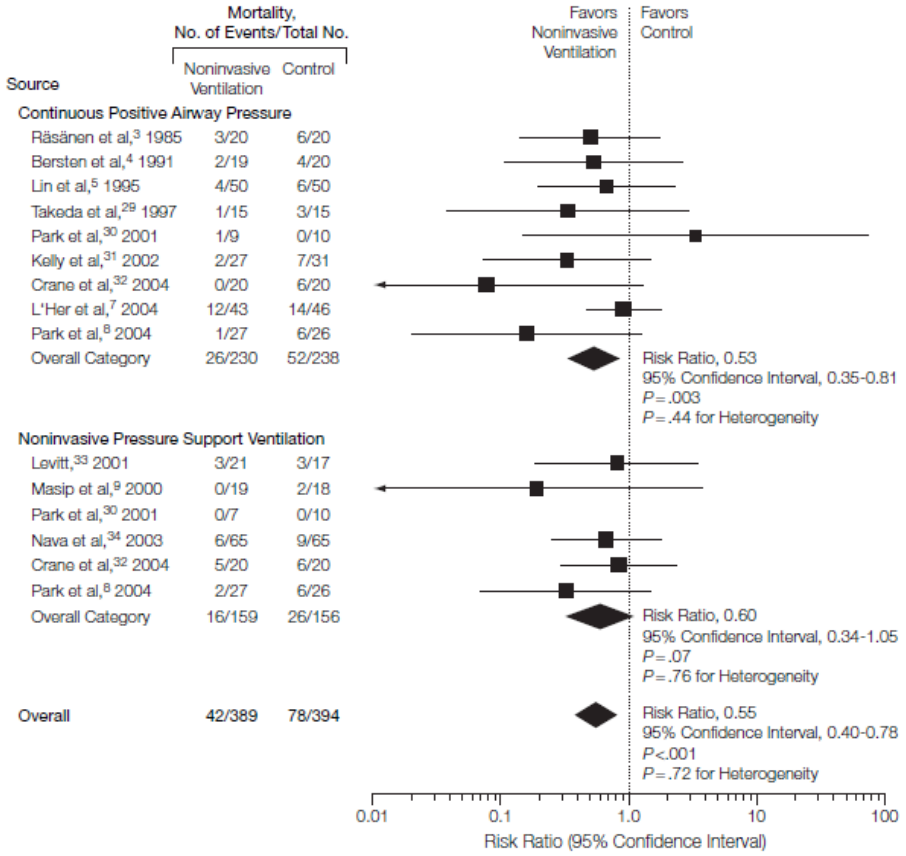
Noninvasive Ventilation in Pulmonary Edema Complicating Acute Myocardial Infarction

Circulation journal

Clinical outcomes in Meta-analysis (Death)



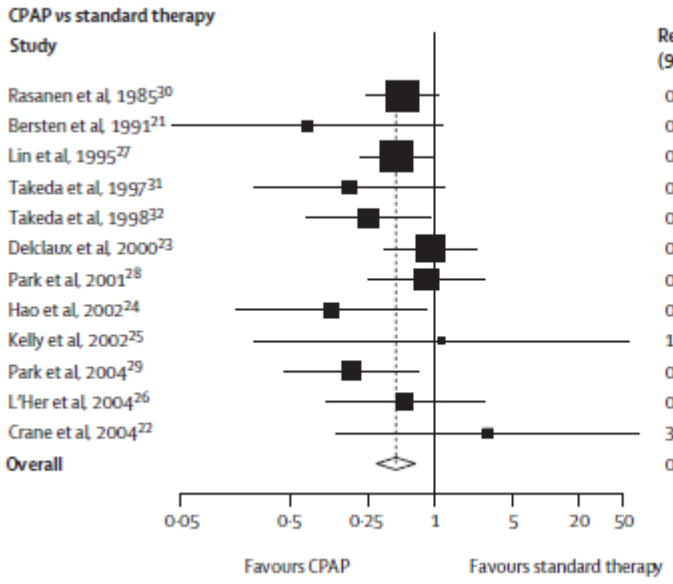
Lancet



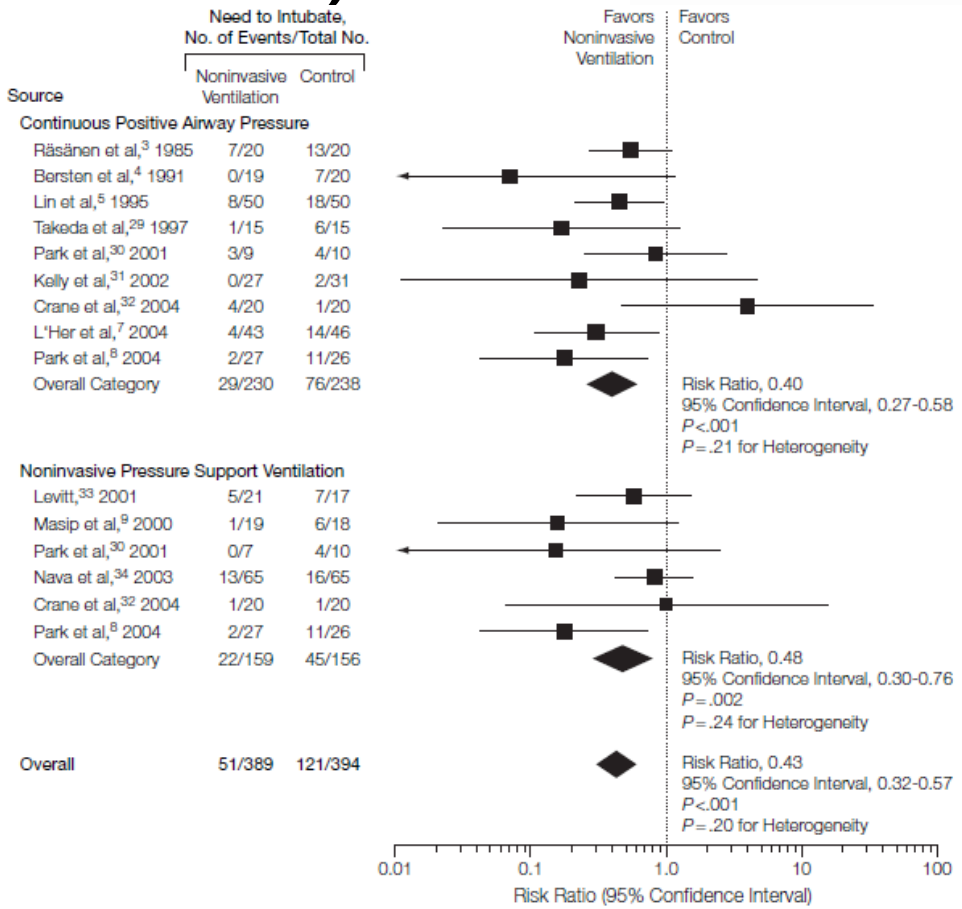
JAMA

Lancet 2006; 367: 1155–63
JAMA. 2005;294:3124-3130

Clinical outcomes in Meta-analysis (Intubation risk)



Lancet



JAMA

Lancet 2006; 367: 1155–63
JAMA. 2005;294:3124-3130

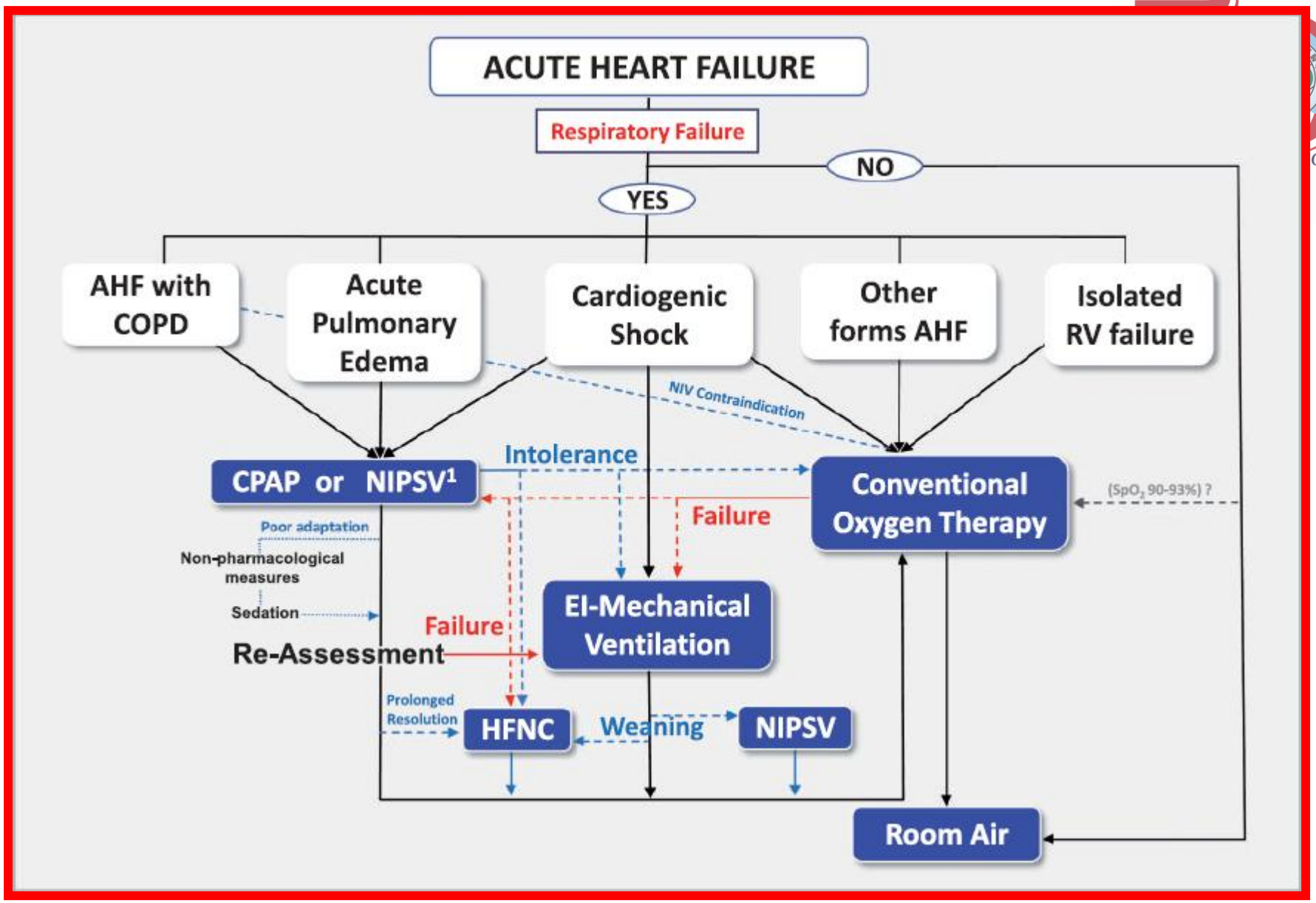
ERS/ATS guidelines

- **We recommend either bilevel NIV or CPAP for patients with ARF due to cardiogenic pulmonary edema**
- **acute coronary syndrome or cardiogenic shock excluded**
- **(Strong recommendation, moderate certainty of evidence.)**

Guidelines

Society	Recommendation	Evidence
ERS/ATS	We recommend either bilevel NIV or CPAP for patients with ARF due to cardiogenic pulmonary oedema.	Strong recommend, moderate evidence
ESC	Non-invasive positive pressure ventilation (CPAP, BiPAP) should be considered in patients with respiratory distress (respiratory rate >25 breaths/min, SpO2 <90%) and started as soon as possible in order to decrease respiratory distress … Blood pressure should be monitored regularly when this treatment is used.	Class: Iia LOE: B
AHA	(No NIV description)	
TSOC	….It is recommended that non-invasive ventilation should be initiated as early as possible in acute heart failure patients with dyspnea and respiratory distress if no obvious contraindication….	No grading

Eur Respir J 2017; 50: 1602426
Eur Heart J. 2016;37:2129–2200
Acta Cardiol Sin 2012;28:161-195



Eur Heart J. 2018 Jan 1;39(1):17-25

Immunocompromised

NONINVASIVE VENTILATION IN IMMUNOSUPPRESSED PATIENTS WITH PULMONARY INFILTRATES, FEVER, AND ACUTE RESPIRATORY FAILURE

GILLES HILBERT, M.D., DIDIER GRUSON, M.D., FRÉDERIC VARGAS, M.D., RUDDY VALENTINO, M.D., GEORGES GBIKPI-BENISSAN, M.D., MICHEL DUPON, M.D., JOSY REIFFERS, M.D., AND JEAN P. CARDINAUD, M.D.

	NIV	Standard	P
	26	26	
intubation	12(46%)	20 (77%)	0.03
died in ICU	10(38%)	18 (69%)	0.03
died in hospital	13(50%)	21 (81%)	0.02

G. HILBERT Et al. NEJM 2001; 344: pp. 481-487

Recommendation

- **We suggest early NIV for immunocompromised patients with ARF.**
- **(Conditional recommendation, moderate certainty of evidence.)**

TABLE 1. BASE-LINE CHARACTERISTICS OF THE PATIENTS.*

CHARACTERISTIC	NONINVASIVE-VENTILATION GROUP (N=26)	STANDARD-TREATMENT GROUP (N=26)
Age — yr	48±14	50±12
Male sex — no. (%)	18 (69)	19 (73)
SAPS II†	45±10	42±9
Respiratory rate — breaths/min	35±3	36±3
Heart rate — beats/min	108±16	111±14
Systolic blood pressure — mm Hg	127±19	123±17
Body temperature — °C	38.3±0.6	38.5±0.6
Microbiologic diagnosis of pneumonia — no. (%)‡	13 (50)	11 (42)
PaO_2:FiO_2	141±24	136±23
$PaCO_2$ — mm Hg	37±4	38±5
Arterial pH	7.45±0.04	7.43±0.04
White-cell count — cells/mm³		
Patients with immunosuppression from hematologic cancer and neutropenia	264±163	241±147
Patients with other types of immunosuppression	9980±5290	10,590±5730
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)

G. HILBERT Et al. NEJM 2001; 344: pp. 481-487

Table 1. Patient Characteristics at Randomization

Characteristic	No. (%) High-Flow Oxygen Therapy (n = 388)	No. (%) Standard Oxygen Therapy (n = 388)
Demographics		
Age, median (IQR), y	64 (55-70)	63 (56-71)
Sex		
Men	270 (69.6)	247 (63.6)
Women	118 (30.4)	141 (36.4)
Comorbidities		
Chronic		
Respiratory[a]	115 (29.6)	127 (32.7)
Heart failure	23 (5.9)	27 (6.9)
Liver	45 (13.3)	56 (14.4)
Kidney disease	73 (18.8)	69 (20.4)
Charlson Comorbidity Index[b]	5 (4-7)	5 (3-7)
Underlying conditions[c]		
Cancer	294 (75.8)	319 (82.2)
Hematologic malignancies	167 (43.0)	181 (46.6)
Solid tumors	127 (32.7)	138 (35.6)
Immunosuppressive drugs	133 (34.3)	135 (34.8)
Non-transplant-related reasons	89 (22.9)	98 (25.2)
After solid organ transplantation	44 (11.3)	37 (9.5)
Time since diagnosis of underlying condition, median (IQR), mo	6.4 (1-29)	7.0 (0.8-40.0)

Table Title:

Patient Characteristics at Randomization

JAMA. 2018;320(20):2099-2107.

JAMA Network™

Effect of High-Flow Nasal Oxygen vs Standard Oxygen on 28-Day Mortality in Immunocompromised Patients With Acute Respiratory Failure: The HIGH Randomized Clinical Trial

JAMA. 2018;320(20):2099-2107. doi:10.1001/jama.2018.14282

Table 2. Primary and Secondary End Points[a]

End Points	No. (%) High-Flow Oxygen Therapy (n = 388)	No. (%) Standard Oxygen Therapy (n = 388)	Mean Difference, % (95% CI)[b]	Relative Difference (95% CI)	*P* Value
Primary					
All-cause day-28 mortality	138 (35.6)	140 (36.1)	−0.5 (−7.3 to 6.3)	HR, 0.98 (0.77 to 1.24)	.94
Secondary					
Invasive mechanical ventilation[c]	150 (38.7)	170 (43.8)	−5.1 (−12.3 to 2.0)	HR, 0.85 (0.68 to 1.06)[d]	.17
ICU-acquired infection	39 (10.0)	41 (10.6)	−0.6 (−4.6 to 4.1)	HR, 1.01 (0.96 to 1.06)[d]	.91
ICU mortality	123 (31.7)	122 (31.4)	0.3 (−6.3 to 6.8)	RR, 1.01 (0.82 to 1.24)	.64
Hospital mortality	160 (41.2)	162 (41.7)	−0.5 (−7.5 to 6.4)	RR, 0.99 (0.84 to 1.17)	.77
Length of stay, median (IQR), d					
ICU	8 (4-14)	6 (4-13)	0.6 (−1.0 to 2.2)	NA[e]	.07
Hospital	24 (14-40)	27 (15-42)	−2 (−7.3 to 3.3)	NA[e]	.60

Abbreviations: HR, hazard ratio; ICU, intensive care unit; IQR, interquartile range; NA, not available; RR, relative risk.

[a] No patients were lost to follow-up.

[b] Mean difference was defined across intervention and controls groups by absolute risk difference for binary outcomes (mortality, invasive mechanical ventilation, infections) and difference in means for quantitative outcomes (lengths of stay in ICU and in hospital).

[c] The use of invasive mechanical ventilation was based on the clinical response to oxygen or noninvasive ventilation, clinical status (including oxygen saturation by pulse oximetry [Spo_2], respiratory rate, signs of respiratory distress, and bronchial secretion volume), and patient adherence to noninvasive ventilation. Criteria for invasive mechanical ventilation were severe hemodynamic instability (requiring norepinephrine or epinephrine >0.3 µg/kg/min) or cardiorespiratory arrest or ongoing myocardial infarction, severe encephalopathy (Glasgow Coma Scale score <11), severe airway secretion retention or worsening of respiratory distress (SpO_2 <92% or respiratory rate >40/min regardless of oxygen flow rate or use of accessory respiratory muscles), inability to maintain Pao_2 greater than 65 mm Hg with fraction of inspired oxygen (Fio_2) greater than 0.6 or dependency on noninvasive ventilation with inability to remain off noninvasive ventilation for longer than 2 hours, greater than 50% increase in the time on noninvasive ventilation from one day to the next (eg, 6 hours of noninvasive ventilation on day 1, then >9 hours on day 2).

[d] Cause-specific HR.

[e] Effect of high-flow oxygen therapy on length-of-stay measures could not be expressed by HRs.

Immunocompromised patients with acute respiratory distress syndrome: secondary analysis of the LUNG SAFE database

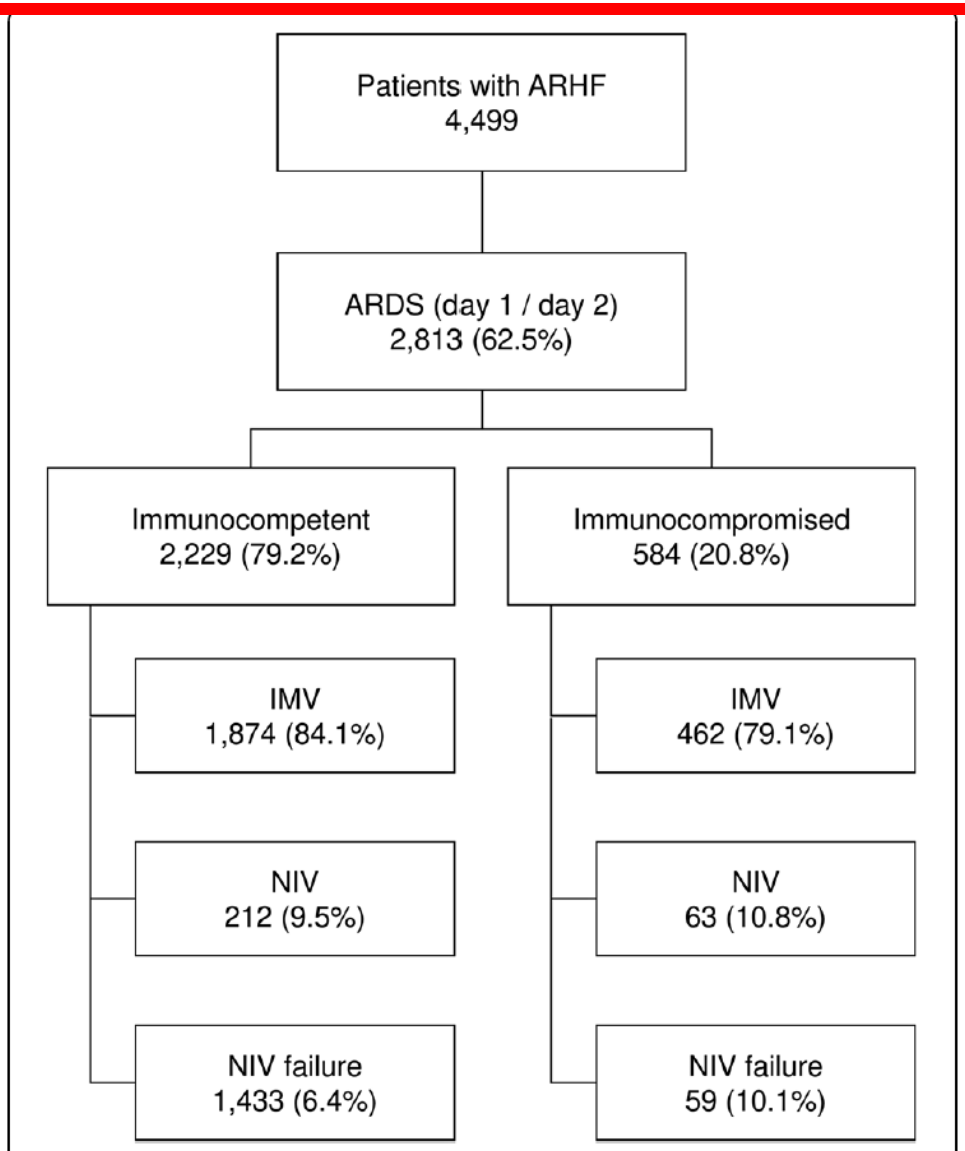


Fig. 1 Flow diagram of the study. Flow diagram showing the

Cortegiani *et al. Critical Care* (2018) 22:157

Table 3 Clinical endpoints in immunocompromised

Clinical endpoints				*p* Value
Duration of mechanical ventilation, d, median (Q_1–Q				0.4352
Progression/regression of ARDS[a], *n* (%)				
No change				0.4449
Progression				0.7199
Regression				**0.0045**
Resolution				**< 0.0001**
Limitation of life-sustaining measures, *n* (%)				
Decision to withhold life-sustaining measures				0.9587
Decision to withdraw life-sustaining measures	10		14 (23.7)	0.9480
Decision to withhold or withdraw life-sustaining measures	154	21 (33.3)	20 (33.9)	0.9962
Before IMV or NIV start	1 (0.6	0 (0.0)	1 (5.0)	0.2062
ICU mortality[d], *n* (%)	214 (46.3)	18 (28.6)[b]	34 (57.6)[c]	**0.0043**
Hospital mortality[e], *n* (%)				
All patients	242 (52.8)	25 (39.7)	37 (62.7)[c]	**0.0362**
Patients with limitations of life-sustaining measures[f]	137 (89.0)	17 (81.0)	19 (95.0)	0.3803

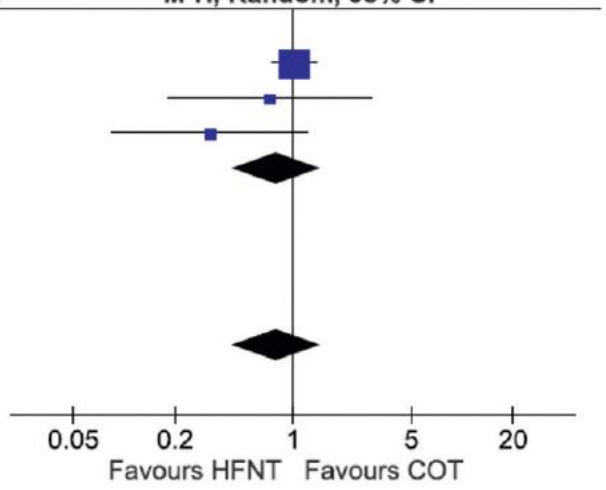
1.NIV 成功的病人有較低的non-pulmonary SOFA score

2.使用IMV的病人死亡率已顯著降低

Cortegiani *et al. Critical Care* (2018) 22:157

High flow nasal therapy in immunocompromised patients with acute respiratory failure: A systematic review and meta-analysis

(a)	HFNT		COT			Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI
1.5.1 ICU mortality						
Azoulay et al. 2018	123	388	122	388	68.5%	1.01 [0.75, 1.37]
Frat et al. 2016	4	26	6	30	15.2%	0.73 [0.18, 2.92]
Roca et al. 2015	10	22	13	18	16.3%	0.32 [0.08, 1.21]
Subtotal (95% CI)		**436**		**436**	**100.0%**	**0.80 [0.44, 1.45]**
Total events	137		141			
Heterogeneity: Tau² = 0.11; Chi² = 2.87, df = 2 (P = 0.24); I² = 30%						
Test for overall effect: Z = 0.74 (P = 0.46)						
Total (95% CI)		**436**		**436**	**100.0%**	**0.80 [0.44, 1.45]**
Total events	137		141			
Heterogeneity: Tau² = 0.11; Chi² = 2.87, df = 2 (P = 0.24); I² = 30%						
Test for overall effect: Z = 0.74 (P = 0.46)						
Test for subgroup differences: Not applicable						

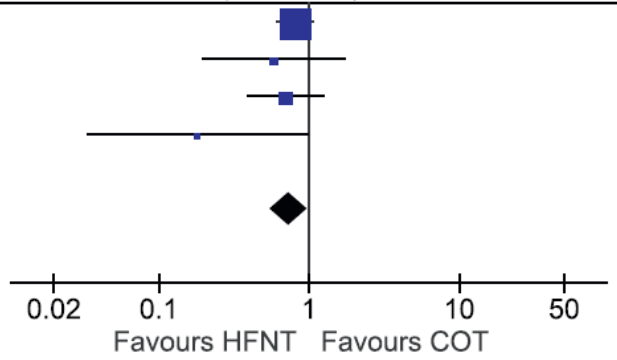


A. Cortegiani et al. / Journal of Critical Care 50 (2019) 250–256

Study or Subgroup	HFNT Events	HFNT Total	COT Events	COT Total	Weight	Odds Ratio M-H, Random, 95% CI
Azoulay et al. 2018	150	388	170	388	69.4%	0.81 [0.61, 1.08]
Frat et al. 2016	8	26	13	30	6.5%	0.58 [0.19, 1.75]
Lemiale et al. 2017	40	90	48	90	21.3%	0.70 [0.39, 1.26]
Roca et al. 2015	13	22	16	18	2.8%	0.18 [0.03, 0.99]
Total (95% CI)		**526**		**526**	**100.0%**	**0.74 [0.55, 0.98]**
Total events	211		247			

Heterogeneity: Tau² = 0.01; Chi² = 3.23, df = 3 (P = 0.36); I² = 7%

Test for overall effect: Z = 2.11 (P = 0.03)



A. Cortegiani et al. / Journal of Critical Care 50 (2019) 250–256

Conclusion

- **Only higher non-pulmonary SOFA score, lower PaO2/ FiO2 ratio and lower improvement of respiratory failure were associated with greater in-hospital mortality**
- **general conditions, underlying pathologies and ARF aetiology may have more importance than oxygenation strategy for the management of immunocompromised patients.**
- **The ability of HFNT to reduce respiratory rate and decrease respiratory distress, dyspnoea and improve oxygenation [24-26], may postpone or avoid the need to intubate giving more time to clinicians to investigate the ARF aetiology and to deliver appropriate treatment.**
- **delaying unavoidable intubation is associated with worse outcomes**

NIV in ARF in the post-operative setting

Acute respiratory failure after OP

- Surgery, particularly that approaching the diaphragm, anaesthesia and post-operative pain → deleterious effects on the respiratory system
- These modifications of respiratory function occur early after surgery and diaphragm dysfunction may last up to 7 days
- use of NIV may increase lung aeration and decrease the amount of atelectasis during the post-operative period of patients undergoing major abdominal surgery
- CPAP and bilevel NIV are effective at improving lung aeration and arterial oxygenation and decreasing the amount of atelectasis without adverse haemodynamic effects during the post-operative period after extubation

Supra-diaphragmatic surgery

- **One RCT in patients with ARF after lung cancer resection**→ NIV decreased the need for re-intubation and reduced hospital mortality.

~ Auriant I, AJRCCM 2001; 164: 1231–1235

- **830 patients following cardiothoracic surgery with or at risk for ARF** →the use of **high-flow nasal cannula** therapy compared with intermittent NIV did not result in a worse rate of re-intubation.

~Stephan F, JAMA 2015; 313: 2331–2339

Abdominal and/or pelvic surgery

- **ARF after abdominal surgery:** NIV resulted in avoidance of intubation in 67% cases, and a reduction in the hospital LOS and mortality, compared with intubated patients

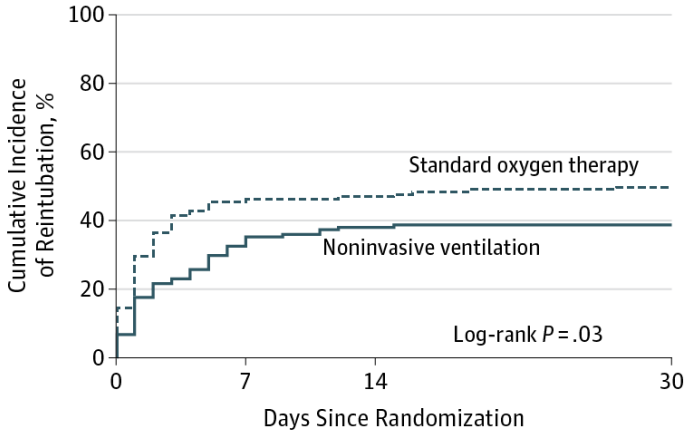
~ Jaber S, Chest 2005; 128: 2688–2695

- **RCT on 40 patients undergoing solid organ transplantation** (mainly liver transplantation) : NIV improved oxygenation and decreased the need for tracheal intubation compared with conventional therapy

~ Antonelli M, JAMA 2000; 283: 235–241

Effect of NIV on Tracheal Reintubation Among Patients With Hypoxemic ARF Following Abdominal Surgery: A Randomized Clinical Trial

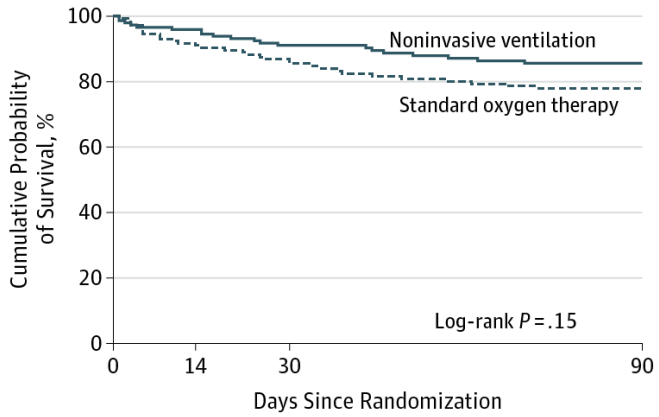
Cumulative Incidence of Reintubation



No. at risk

Standard oxygen therapy	145	79	76	71
Noninvasive ventilation	148	99	90	87

Probability of Survival



No. at risk

Standard oxygen therapy	145	132	125	102
Noninvasive ventilation	148	141	131	109

Jaber S, JAMA. 2016;315(13):1345-1353

NIV in the treatment of ARF in postoperative patients

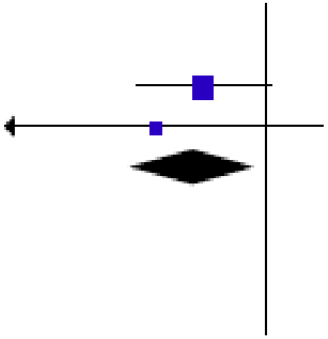
Mortality

1.1.2 Treatment of ARF in postop patients

Auriant 2001	3	24	9	24	38.3%	0.33 [0.10, 1.08]
Squadrone 2005	0	105	3	104	14.9%	0.14 [0.01, 2.71]
Subtotal (95% CI)		**129**		**128**	**53.2%**	**0.28 [0.09, 0.84]**
Total events	3		12			

Heterogeneity: $Chi^2 = 0.29$, df = 1 (P = 0.59); $I^2 = 0\%$

Test for overall effect: Z = 2.28 (P = 0.02)



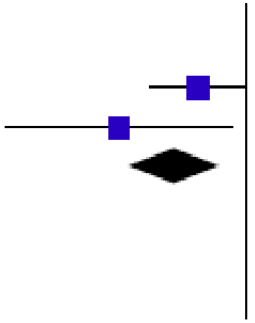
Intubation

1.2.2 Treatment of ARF in postop patients

Auriant 2001	5	24	12	24	42.9%	0.42 [0.17, 1.00]
Squadrone 2005	1	105	10	104	35.9%	0.10 [0.01, 0.76]
Subtotal (95% CI)		**129**		**128**	**78.9%**	**0.27 [0.12, 0.61]**
Total events	6		22			

Heterogeneity: $Chi^2 = 1.85$, df = 1 (P = 0.17); $I^2 = 46\%$

Test for overall effect: Z = 3.13 (P = 0.002)



Recommendation

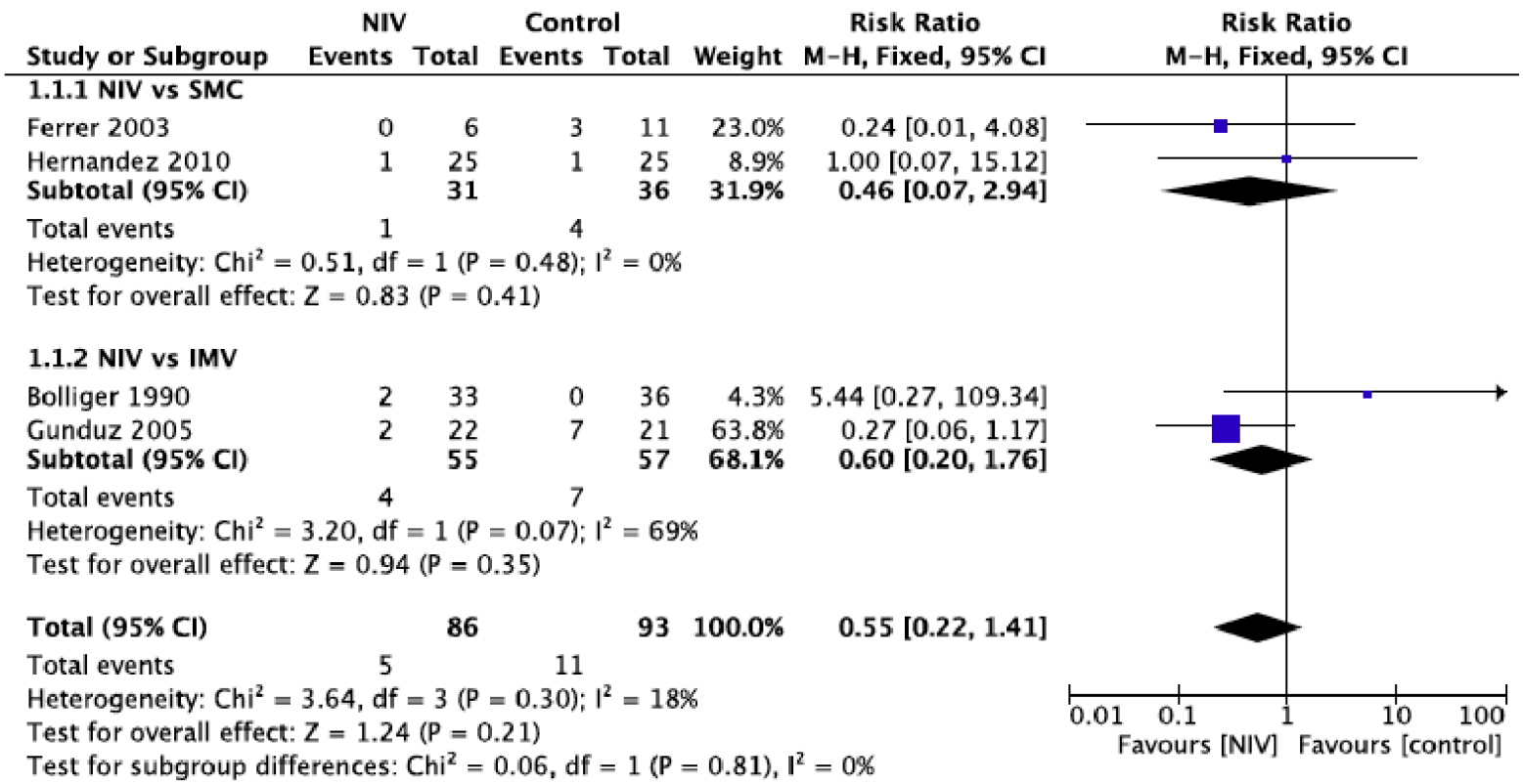
We suggest NIV for patients with post-operative ARF.

(Conditional recommendation, moderate certainty of evidence.)

- **Improve outcomes in patients with abdominal and thoracic surgery, but also after cardiac surgery.**
- **NIV reduces intubation rates, nosocomial infections, lengths of stay, morbidity and mortality.**
- **surgical complications such as anastomotic leak or intra-abdominal sepsis should be addressed first.**
- **cooperative and able to protect the airway**

NIV be used in acute respiratory failure due trauma?

Mortality

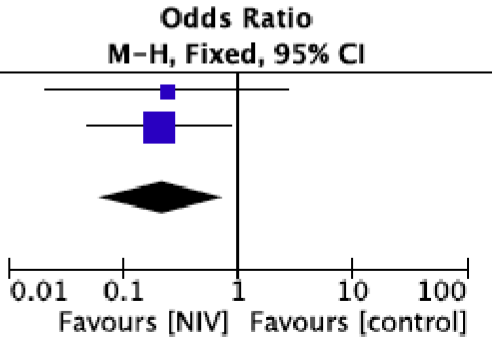

NIV
Control
Risk Ratio
Risk Ratio
Study or Subgroup Events Total Events Total Weight M-H, Fixed, 95% CI
M-H, Fixed, 95% CI
1.1.1 NIV vs SMC
Ferrer 2003 0 6 3 11 23.0% 0.24 [0.01, 4.08]
Hernandez 2010 1 25 1 25 8.9% 1.00 [0.07, 15.12]
Subtotal (95% CI) 31 36 31.9% 0.46 [0.07, 2.94]
Total events 1 4
Heterogeneity: Chi² = 0.51, df = 1 (P = 0.48); I² = 0%
Test for overall effect: Z = 0.83 (P = 0.41)
1.1.2 NIV vs IMV
Bolliger 1990 2 33 0 36 4.3% 5.44 [0.27, 109.34]
Gunduz 2005 2 22 7 21 63.8% 0.27 [0.06, 1.17]
Subtotal (95% CI) 55 57 68.1% 0.60 [0.20, 1.76]
Total events 4 7
Heterogeneity: Chi² = 3.20, df = 1 (P = 0.07); I² = 69%
Test for overall effect: Z = 0.94 (P = 0.35)
Total (95% CI) 86 93 100.0% 0.55 [0.22, 1.41]
Total events 5 11
Heterogeneity: Chi² = 3.64, df = 3 (P = 0.30); I² = 18%
Test for overall effect: Z = 1.24 (P = 0.21)
Test for subgroup differences: Chi² = 0.06, df = 1 (P = 0.81), I² = 0%
0.01 0.1 1 10 100
Favours [NIV] Favours [control]

Intubation

Study or Subgroup	NIV Events	NIV Total	Control Events	Control Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Ferrer 2003	1	6	5	11	25.1%	0.24 [0.02, 2.79]
Hernandez 2010	3	25	10	25	74.9%	0.20 [0.05, 0.87]
Total (95% CI)		**31**		**36**	**100.0%**	**0.21 [0.06, 0.74]**
Total events	4		15			

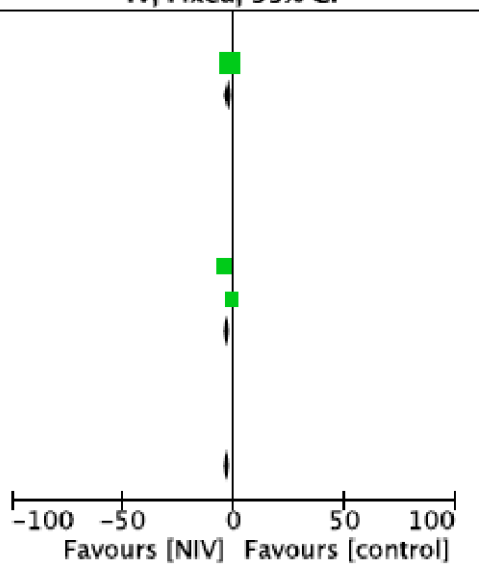
Heterogeneity: $Chi^2 = 0.01$, $df = 1$ ($P = 0.91$); $I^2 = 0\%$

Test for overall effect: $Z = 2.43$ ($P = 0.02$)

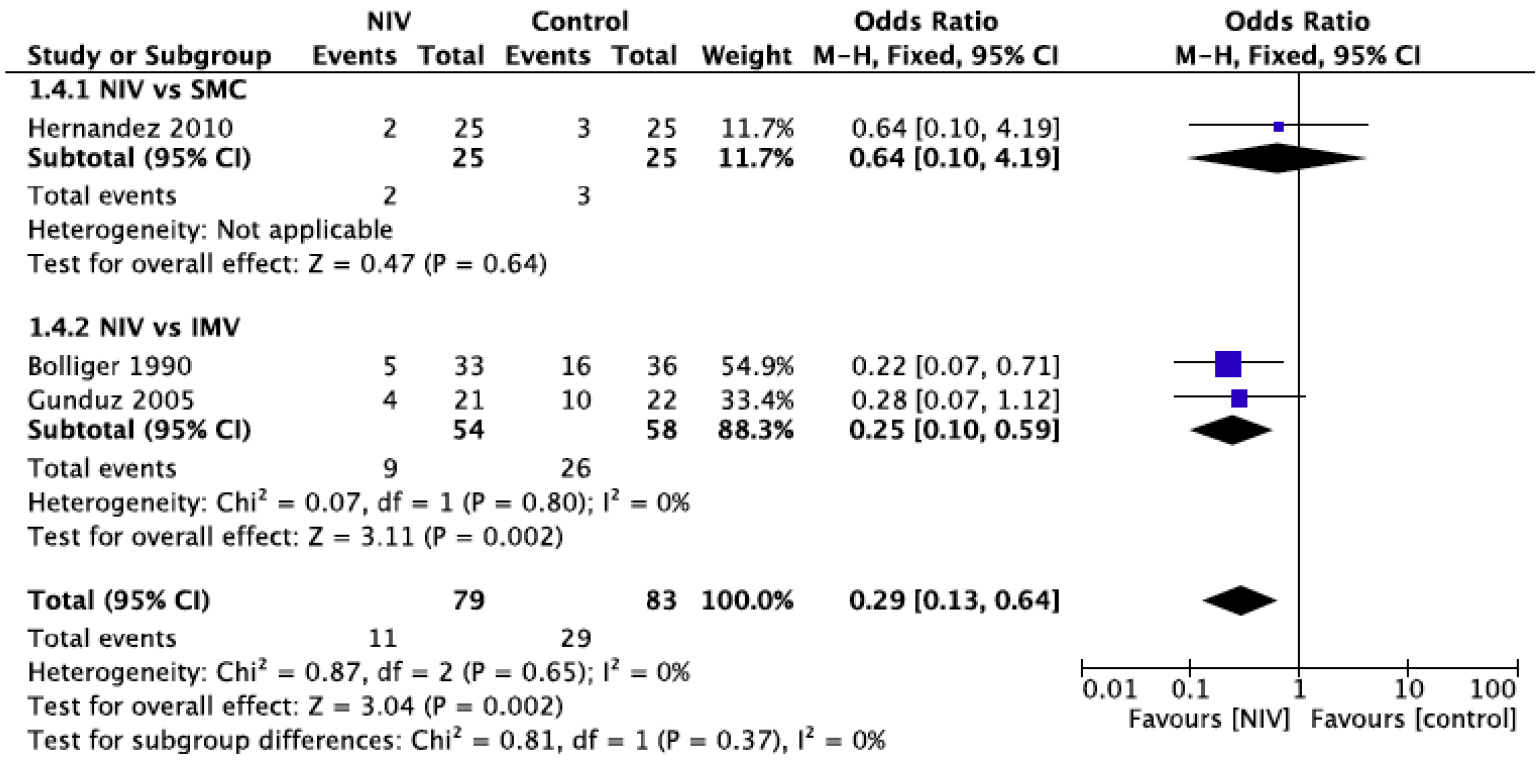


ICU Length of Stay

Study or Subgroup	NIV Mean	NIV SD	NIV Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Fixed, 95% CI
1.3.1 NIV vs SMC								
Hernandez 2010	6	2	25	8	3	25	47.5%	-2.00 [-3.41, -0.59]
Subtotal (95% CI)			**25**			**25**	**47.5%**	**-2.00 [-3.41, -0.59]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.77 (P = 0.006)								
1.3.2 NIV vs IMV								
Bolliger 1990	5.3	2.9	33	9.5	4.4	36	31.2%	-4.20 [-5.94, -2.46]
Gunduz 2005	15	4	22	16	3	21	21.4%	-1.00 [-3.11, 1.11]
Subtotal (95% CI)			**55**			**57**	**52.5%**	**-2.90 [-4.24, -1.55]**
Heterogeneity: $Chi^2 = 5.26$, df = 1 (P = 0.02); $I^2 = 81\%$								
Test for overall effect: Z = 4.23 (P < 0.0001)								
Total (95% CI)			**80**			**82**	**100.0%**	**-2.47 [-3.45, -1.50]**
Heterogeneity: $Chi^2 = 6.07$, df = 2 (P = 0.05); $I^2 = 67\%$								
Test for overall effect: Z = 4.97 (P < 0.00001)								
Test for subgroup differences: $Chi^2 = 0.81$, df = 1 (P = 0.37), $I^2 = 0\%$								



Nosocomial Pneumonia



Recommendation

We suggest NIV for chest trauma patients with ARF.

(Conditional recommendation, moderate certainty of evidence.)

2019台灣胸腔暨重症加護醫學會夏季會

2019 Summer Workshop of Taiwan Society of Pulmonary and Critical Care Medicine

NIV use immediate after cardiac surgery

~ Braz J Cardiovasc Surg 2017;32(4):301-11ORIGINAL

Factors associated with post cardiac surgery pulmonary dysfunction

Preoperative
- Chronic obstructive pulmonary disease[17-21]
- Obesity[17,22-24]
- Age: >60 years,[25,26] >70 years,[19,20,23] >80 years[17,22,27,28]
- Diabetes[29]
- History of smoking[18,29,30]
- Chronic heart failure[17,20,22,29,31-33]
- Emergency surgery[22,23,25,34]
- Previous cardiac surgery[20,25]
- Immobility[35]

Intraoperative
- Respiratory depression[36]
- Neurological injury[37]
- Lung deflation[38]
- Cardiopulmonary bypass[36,39]
- Topical cooling[40,41]
- Internal mammary artery dissection[15,36,42-47]
- Sternotomy incision[48,49]
- Increased number of bypass grafts[44,50,51]
- Increased duration of cardiopulmonary bypass[22,23,31,34,44,50,52]
- Lower core temperature[22,34,50,53]

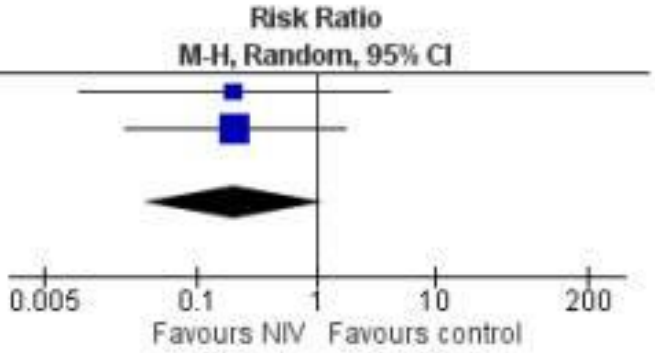
Postoperative
- Respiratory depression associated with nonreversal of anesthesia[36]
- Phrenic nerve dysfunction[54]
- Diaphragmatic dysfunction[55,56]
- Pain[57-60]
- Constant tidal volumes/short shallow respiration[48]
- Reduced compliance[61]
- Reduced vital capacity and functional residual capacity[62]
- Ventilation-perfusion mismatch and physiological shunt[36,63,64]
- Fluid imbalance[27,31,39,65]
- Immobility,[66,67] position[68]
- Chest tubes[69]
- Nasogastric tubes[70]
- Impaired mucocilliary clearance,[71] ineffective cough[14,72]
- Pleural effusion[47,73,74]
- Atelectasis[72,75-77]
- Pulmonary edema[4,7,78,79]
- Aspiration[80]

~ Am J Crit Care September 2004 vol. 13 no. 5 384-393

Pneumonia

Study or Subgroup	NIV Events	NIV Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
Al Jaaly et al.[15], 2013	0	63	2	63	33.5%	0.20 [0.01, 4.08]
Zarbock et al.[10], 2009	1	232	5	236	66.5%	0.20 [0.02, 1.73]
Total (95% CI)		**295**		**299**	**100.0%**	**0.20 [0.04, 1.16]**
Total events	1		7			

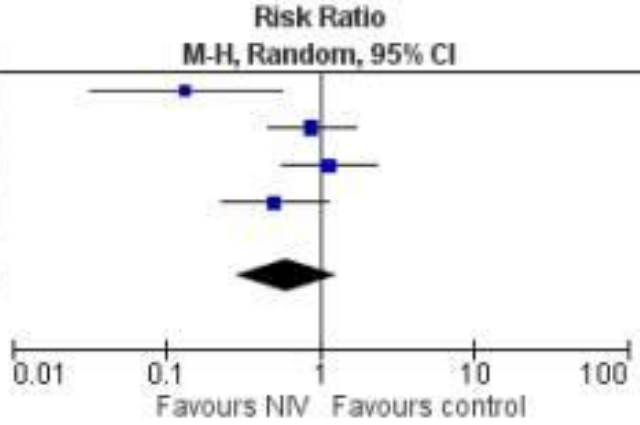
Heterogeneity: Tau² = 0.00; Chi² = 0.00, df = 1 (P = 0.99); I² = 0%
Test for overall effect: Z = 1.79 (P = 0.07)



Atelectasis

Study or Subgroup	NIV Events	NIV Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
Al Jaaly et al.[15], 2013	2	63	15	63	16.0%	0.13 [0.03, 0.56]
Franco et al.[16], 2011	7	13	8	13	29.2%	0.88 [0.45, 1.70]
Jousela et al.[11], 1994	8	15	7	15	28.1%	1.14 [0.56, 2.35]
Matte et al.[3], 2000	10	66	9	30	26.7%	0.51 [0.23, 1.11]
Total (95% CI)		**157**		**121**	**100.0%**	**0.60 [0.28, 1.28]**
Total events	27		39			

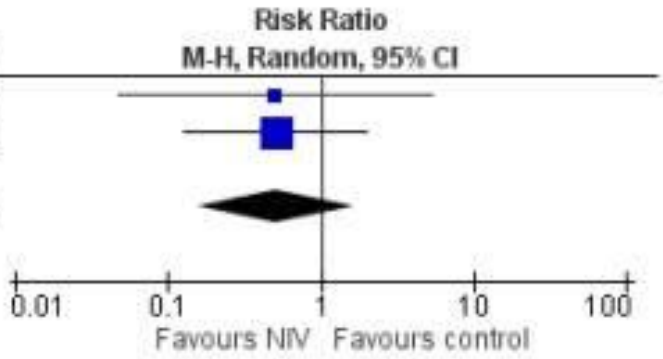
Heterogeneity: Tau² = 0.39; Chi² = 9.70, df = 3 (P = 0.02); I² = 69%
Test for overall effect: Z = 1.31 (P = 0.19)



Re-intubation

Study or Subgroup	NIV Events	NIV Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
Al Jaaly et al.[15], 2013	1	63	2	63	25.1%	0.50 [0.05, 5.38]
Zarbock et al.[10], 2009	3	232	6	236	74.9%	0.51 [0.13, 2.01]
Total (95% CI)		**295**		**299**	**100.0%**	**0.51 [0.15, 1.66]**
Total events	4		8			

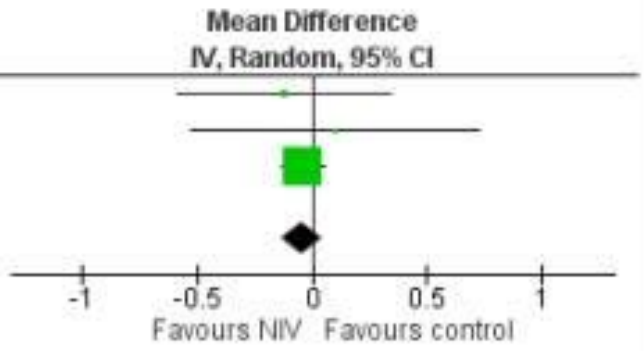
Heterogeneity: Tau² = 0.00; Chi² = 0.00, df = 1 (P = 0.99); I² = 0%
Test for overall effect: Z = 1.12 (P = 0.26)



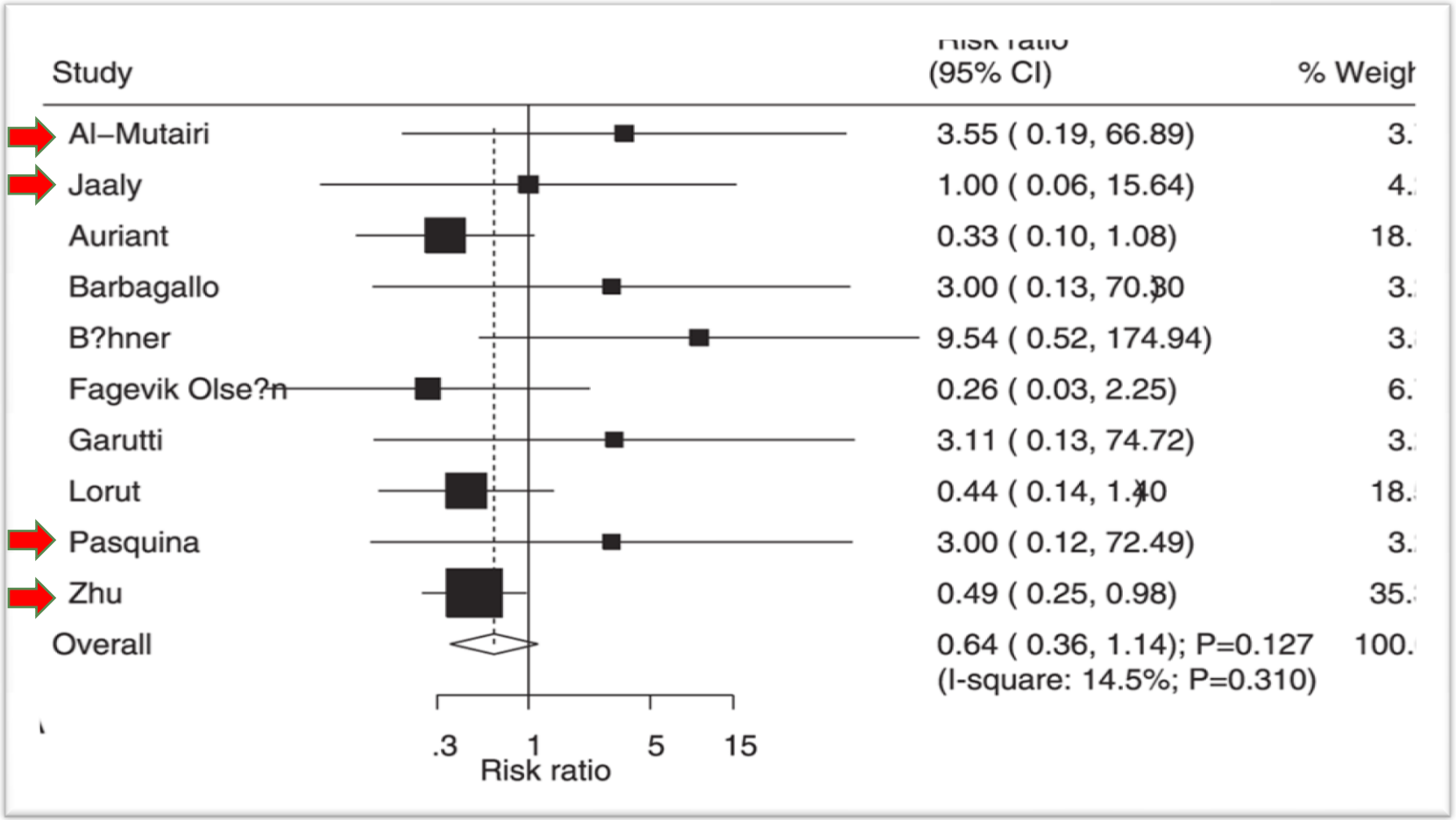
ICU stay

Study or Subgroup	NIV Mean	NIV SD	NIV Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Random, 95% CI
Matte et al.[3], 2000	2.09	0.5	33	2.21	1.2	30	3.7%	-0.12 [-0.58, 0.34]
Pinilla et al.[17], 1990	2.8	1.1	32	2.7	1.3	26	2.0%	0.10 [-0.53, 0.73]
Zarbock et al.[10], 2009	1.12	0.7	232	1.16	0.1	236	94.4%	-0.04 [-0.13, 0.05]
Total (95% CI)			**297**			**292**	**100.0%**	**-0.04 [-0.13, 0.05]**

Heterogeneity: Tau² = 0.00; Chi² = 0.31, df = 2 (P = 0.86); I² = 0%
Test for overall effect: Z = 0.89 (P = 0.37)

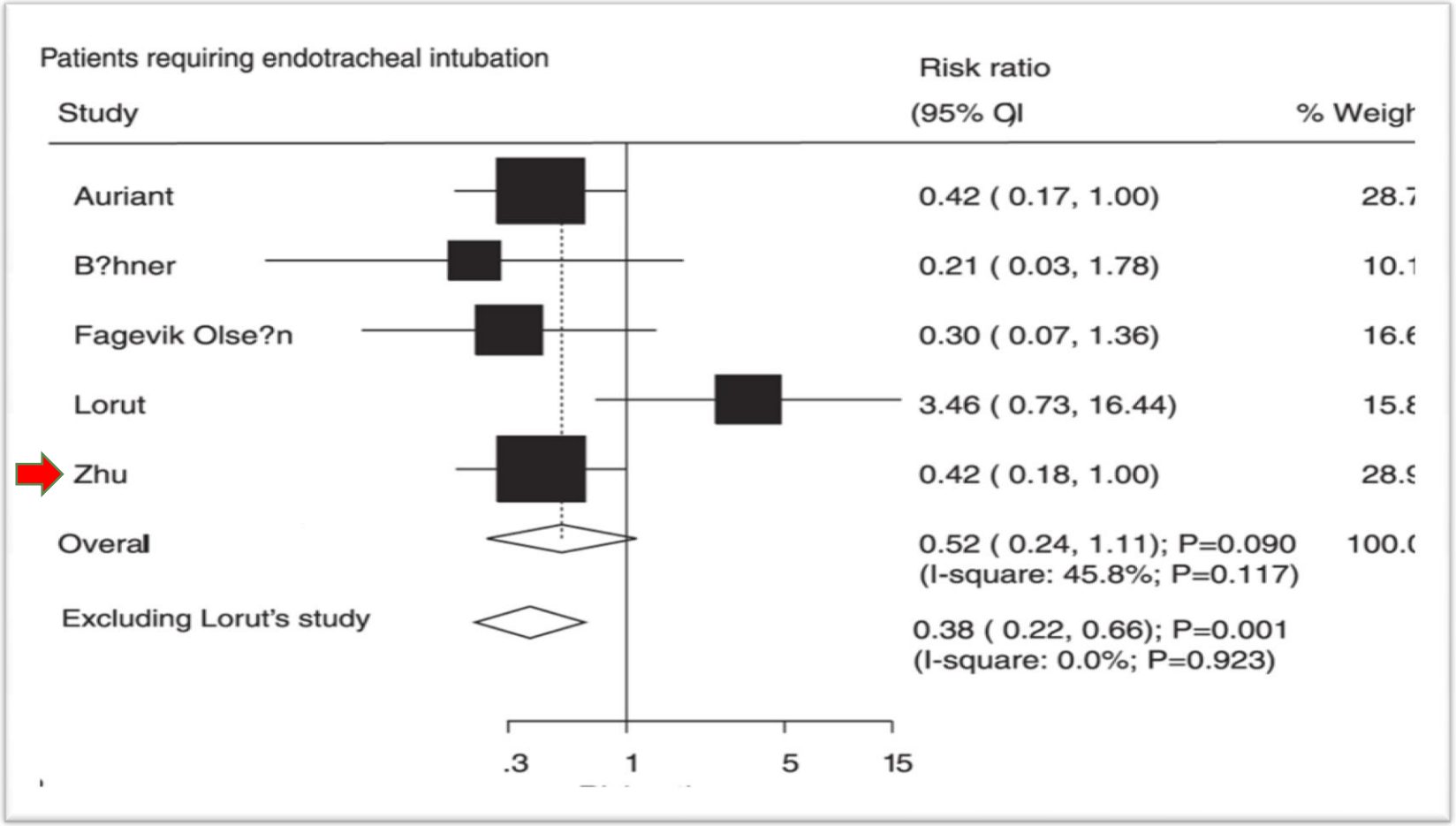


Similar mortality with immediate postoperative NIV use



~ Medicine (2016) 95:38

Fewer re-intubation with immediate postoperative NIV



~ Medicine (2016) 95:38

2019台灣胸腔暨重症加護醫學會夏季會
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NIV to treat acute post-operative respiratory failure after cardiac surgery

Does BiPAP improve outcome of acute respiratory failure after open-heart surgery?

- 44 patients, group I: IV, group: BiPAP

- HR: higher in Group I at 30 and 60 min and at 12 and 24 h
- MAP, SpO_2: higher in Group I also
- RR, $PaCO_2$showed significant higher in Group II
- MV duration: Group I > Group II
- Complications were statistically insignificant between Group I and Group II.

~ Ann Card Anaesth 2017;20:416-21

Variable	Univariate Analysis	
	Adjusted OR (95% CI)*	*P*
Sex		
Males	1.45 (0.44–4.76)	.54
Females	Reference group	
Age, y	1.09 (1.01–1.17)	.03
BMI	0.90 (0.80–1.02)	.09
EuroSCORE II	1.20 (1.03–1.39)	.02
Estimated glomerular filtration rate	1.02 (0.99–1.04)	.36
Smoking status		
Current smoker	0.49 (0.11–2.29)	.37
Ex-smoker or never smoker	Reference group	
Hypertension	1.52 (0.32–7.15)	.60
Chronic atrial fibrillation	3.95 (1.27–12.28)	.02
Diabetes mellitus	1.35 (0.48–3.81)	.58
Dyslipidemia	0.56 (0.19–1.60)	.28
Stroke	1.91 (0.37–9.71)	.44
COPD	4.38 (1.49–12.83)	.004
Peripheral vascular disease	0.70 (0.15–3.28)	.65
Heart failure (NYHA ≥ 2)	3.54 (1.01–13.02)	.04
Left ventricle ejection fraction	0.96 (0.92–1.01)	.11
Cardiopulmonary bypass time	1.00 (0.99–1.01)	.70
Type of operation		
Coronary artery bypass grafting	1.73 (0.60–4.97)	.31
Other	Reference group	
Complexity of operation		
Combined	1.82 (0.22–14.90)	.57
Noncombined	Reference group	
Postoperative complications		
Low cardiac output syndrome	2.16 (0.42–11.20)	.25
Postoperative stroke	3.69 (1.77–13.01)	.002
Renal replacement therapy	8.80 (1.03–23.06)	<.001

~ RESPIRATORY CARE Paper in Press. Published on April 2, 2019

2019台灣胸腔暨重症加護醫學會夏季會
2019 Summer Workshop of Taiwan Society of Pulmonary and Critical Care Medicine

Palliative care

Noninvasive Ventilation in Patients With Do-Not-Intubate and Comfort-Measures-Only Orders: A Systematic Review and Meta-Analysis*

- 2,020 patients with acute respiratory failure & DNI orders
- **Hospital discharge** survival rate: **56%** (95% CI, 49-64%)

  1 year Survival rate: **32%** (95% CI, 21-45%)
- **Hospital survival :**

  COPD :68%

  Pulmonary edema: 68%,

  Pneumonia:41%

  Malignancy.:37%
- Survival was comparable in hospital ward versus an ICU.
- Quality of life of survivors was not reduced compared with baseline

Wilson ME et al. Crit Care Med. 2018 Aug;46(8):1209-1216

Recommendation

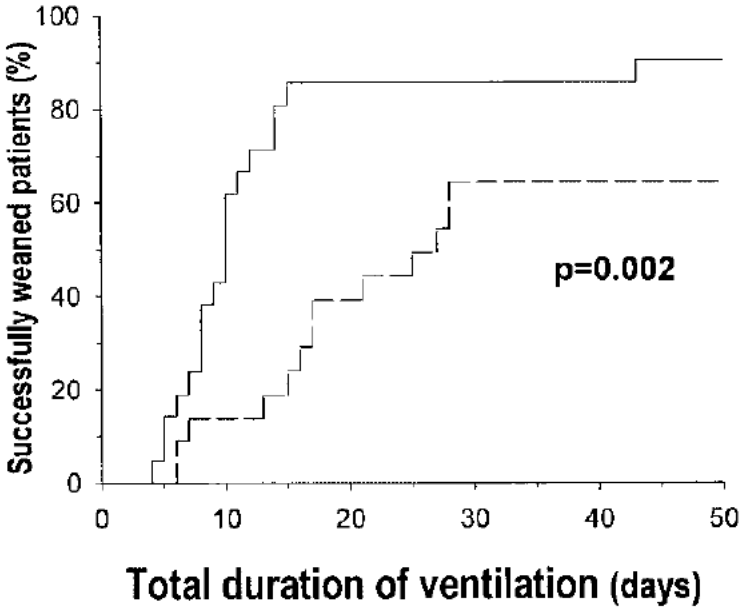
- We suggest offering NIV to dyspneic patients for palliation in the setting of terminal cancer or other terminal conditions.
- (Conditional recommendation, moderate certainty of evidence.)

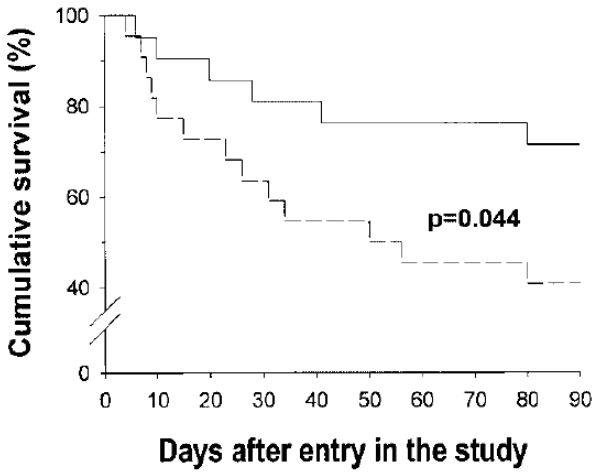
- **Should NIV be used to facilitate weaning patients from invasive mechanical ventilation?**

Noninvasive Ventilation during Persistent Weaning Failure

A Randomized Controlled Trial

Miquel Ferrer, Antonio Esquinas, Francisco Arancibia, Torsten Thomas Bauer, Gumersindo Gonzalez, Andres Carrillo, Robert Rodriguez-Roisin, and Antoni Torres





In conclusion, NIV is effective to shorten the period of invasive ventilation in patients with persistent weaning failure, and, in consequence, to decrease the incidence of nosocomially acquired infections, mortality, and other outcome parameters such as length of ICU and hospital stays. Am J Respir Crit Care Med Vol 168. pp 70–76, 2003

TABLE 1. BASELINE CHARACTERISTICS OF PATIENTS AT ENTRY INTO THE STUDY

	NIV Group ($n = 21$)	Conventional-Weaning Group ($n = 22$)	p Value
Age, yr	70.3 ± 7.5	71.0 ± 7.2	0.767
Sex, M/F	13/8	17/5	0.444
Current or former smoker, n (%)	13 (62)	17 (77)	0.444
Current or former alcohol abuse, n (%)	4 (19)	2 (9)	0.412
APACHE-II on admission	17.8 ± 4.6	18.5 ± 3.9	0.589
Duration of ICU stay, d	7.3 ± 2.8	7.5 ± 3.9	0.801
Duration of mechanical ventilation, d	7.1 ± 2.8	7.0 ± 3.4	0.959
Number of comorbidities per patient	1.8 ± 0.9	1.8 ± 0.9	0.894
White blood cells, $\times 10^9$/L	12.1 ± 4.3	12.4 ± 3.0	0.794
Hematocrit, L/L	0.38 ± 0.07	0.35 ± 0.05	0.170
Patients with chronic pulmonary disorders, n (%)	16 (76)	17 (77)	1.000
Causes of mechanical ventilation, n			0.545
Exacerbation of chronic pulmonary disorders	10	9	
Congestive heart failure	4	5	
Community-acquired pneumonia	2	4	
Hospital-acquired pneumonia	1	1	
Postoperative respiratory failure	–	2	
Acute lung injury	1	1	
Thoracic trauma	1	–	
Hemoptisis	1	–	
Cardiac arrest	1	–	

Definition of abbreviations: APACHE-II = acute physiology and chronic health evaluation-II score; ICU = intensive care unit; NIV = noninvasive ventilation.

Values are means ± SD.

Am J Respir Crit Care Med Vol 168. pp 70–76, 2003

TABLE 3. WEANING RESULTS, LENGTH OF STAY, OUTCOME VARIABLES, AND CAUSES OF DEATH FOR THE NONINVASIVE VENTILATION AND THE CONVENTIONAL-WEANING GROUPS

	NIV Group (*n* = *21*)	Conventional-Weaning Group (*n* = *22*)	p Value
Duration of invasive ventilation, d	9.5 ± 8.3	20.1 ± 13.1	0.003
Total period of ventilatory support*, d	11.4 ± 8.0	20.1 ± 13.1	0.012
ICU stay, d	14.1 ± 9.2	25.0 ± 12.5	0.002
Hospital stay, d	27.8 ± 14.6	40.8 ± 21.4	0.026
Reintubation, n (%)	3 (14)	6 (27)	0.457
Main causes of reintubation, n			
Severe persistent hypoxemia	1	3	
Severe dyspnea	–	2	
Inability to manage secretions	2	–	
Hemodynamic instability	–	1	
Tracheotomy, n (%)	1 (5)	13 (59)	<0.001
ICU survival, n (%)	19 (90)	13 (59)	0.045
Causes of death within 90 d after entry in the study			
Septic shock/MOF	1	9	
Refractory hypoxemia	1	2	
Cardiac arrest	2	1	
Pneumothorax	–	1	
Stroke	1	–	
Pulmonary embolism	1	–	

Definition of abbreviations: ICU = intensive care unit; MOF = multiple organ failure; NIV = noninvasive ventilation.

Values are means ± SD.

*Computation of the total period of ventilatory support in the NIV group was done by the addition of the number of days when both noninvasive and invasive mechanical ventilation were received. In reintubated patients from both groups, the days without ventilatory support between extubation and reintubation were not computed as ventilation days.

TABLE 4. SERIOUS COMPLICATIONS DIAGNOSED IN THE INTENSIVE CARE UNIT AFTER ENTRY INTO THE STUDY

	NIV Group (*n* = 21)	Conventional-Weaning Group (*n* = 22)	p Value
Total number of patients	5	16	0.004
Nosocomial pneumonia	5	13	0.042
Catheter-related sepsis	–	2	–
Sacrum-infected ulcer	–	1	–
Urinary tract infection	–	1	–
Chest wall abscess	–	1	–
Gastrointestinal bleeding	1	–	–
Pneumothorax	–	1	–
Septic shock	2	9	0.045

Definition of abbreviation: NIV = noninvasive ventilation.

Am J Respir Crit Care Med Vol 168. pp 70–76, 2003

TABLE 5. UNIVARIATE AND MULTIVARIATE ANALYSES OF INTENSIVE CARE UNIT AND 90-DAY SURVIVAL

	Adjusted Odds Ratio	95% CI	p Value	Adjusted Odds Ratio	95% CI	p Value
Decreased ICU survival	Univariate analysis			Multivariate analysis		
Conventional-weaning approach	6.6	1.2–35.6	0.029	6.6	1.1–38.8	0.035
Age > 70 yr	5.8	1.1–31.3	0.041	–	–	NS
Decreased 90-d survival	Univariate analysis			Multivariate analysis		
Conventional-weaning approach	–	–	0.044	3.5	1.2–9.6	0.018
Age > 70 yr	–	–	0.012	5.1	1.7–15.0	0.003
Pa_{CO_2} during spontaneous breathing > 45 mm Hg	–	–	0.018	5.8	1.8–18.7	0.003

Definition of abbreviations: CI = confidence interval; ICU = intensive care unit; NS = not significant.

Am J Respir Crit Care Med Vol 168. pp 70–76, 2003

Noninvasive Ventilation as a Systematic Extubation and Weaning Technique in Acute-on-Chronic Respiratory Failure

A Prospective, Randomized Controlled Study

NIV, initially lasting from 2 to 4 h, with nasal oxygen therapy, initially lasting from 1 to 2 h

CHA

Age, yr			
Type of CR			
COPD			
Restrictiv			
Mixed			
Previous cond			
LTO		6	
Home NIV	0	1	
Intubation*	5	7	
FEV$_1$, L†	0.8 ± 0.28	0.95 ± 0.45	NS
FEV$_1$, % pred†	30.4 ± 12.07	38 ± 14	NS
VC, L†	1.69 ± 0.62	1.89 ± 0.88	NS
VC, % pred†	48.45 ± 15.56	64 ± 24.33	NS
FEV$_1$/VC†	45.3 ± 13.43	49.64 ± 10.77	NS
TLC, L†	5.41 ± 2.31	4.54 ± 2.77	NS
TLC, % pred†	89.7 ± 36.1	80.09 ± 35.66	NS
SAPS II	39.25 ± 11.66	37.59 ± 9.77	NS
Pa_{O_2}, kPa‡	8.61 ± 6.10	9.76 ± 6.14	NS
Pa_{CO_2}, kPa‡	10.93 ± 4.05	11.40 ± 4.41	NS
pH‡	7.24 ± 0.12	7.26 ± 0.10	NS

Girault C et al, Am J Respir Crit Care Med 1999; 160(1):86-92.

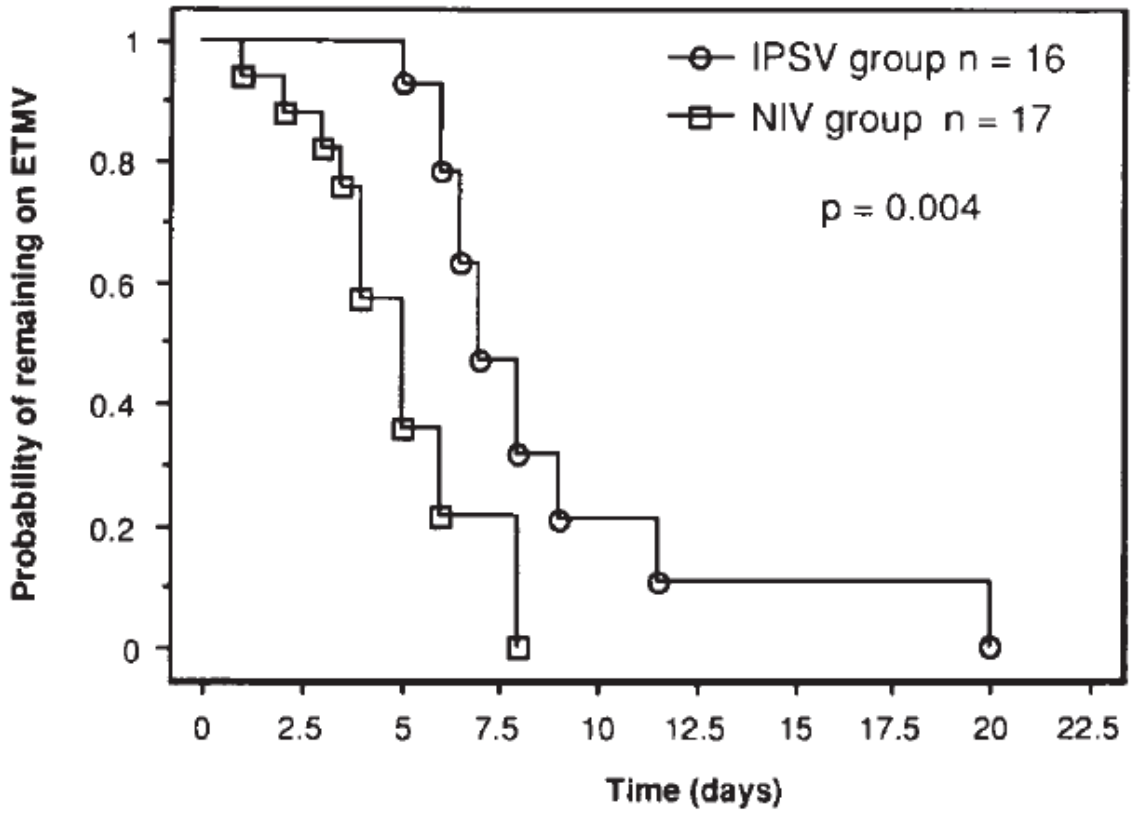
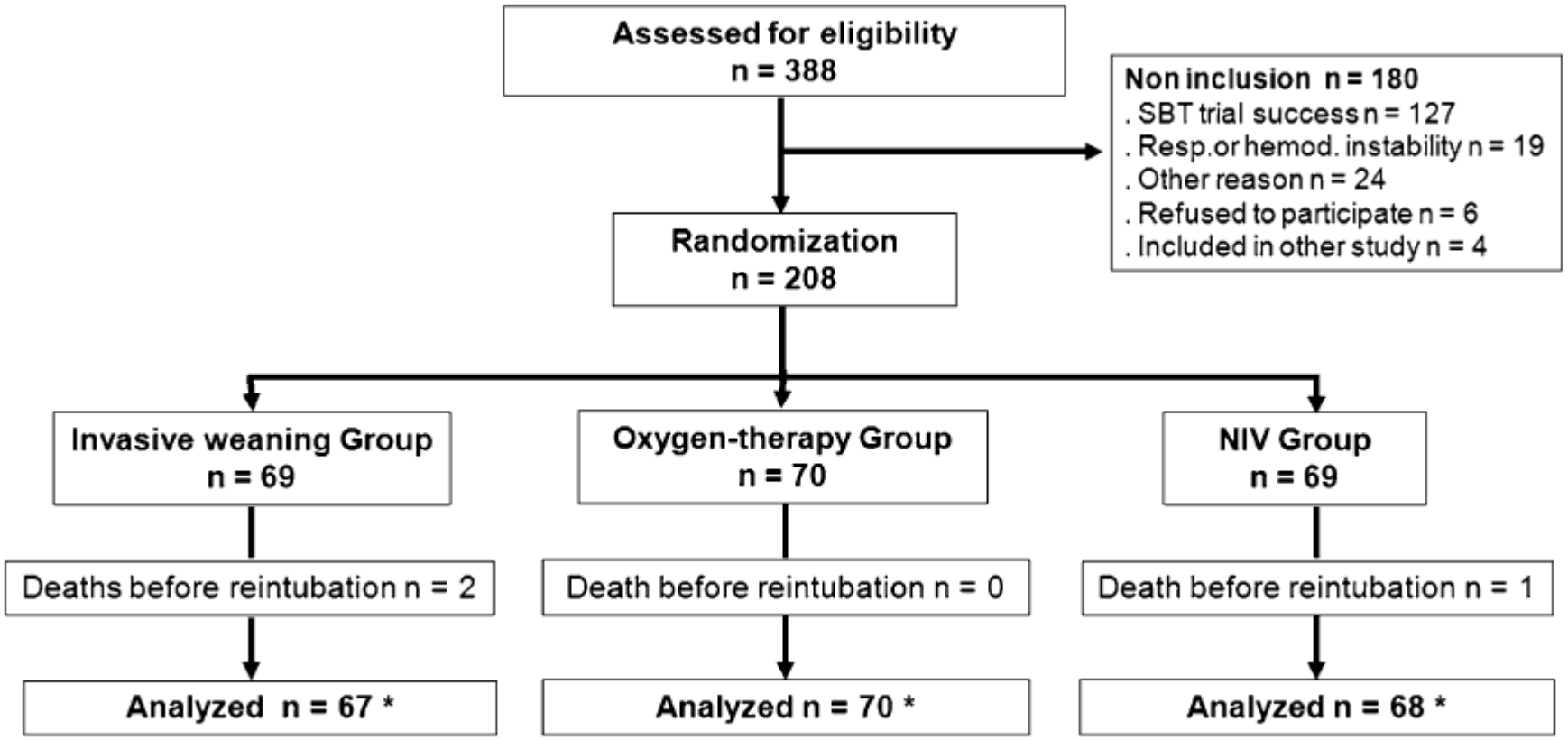


Figure 1. Cumulative probability of remaining on ETMV in the IPSV and NIV weaning groups. IPSV = invasive pressure support

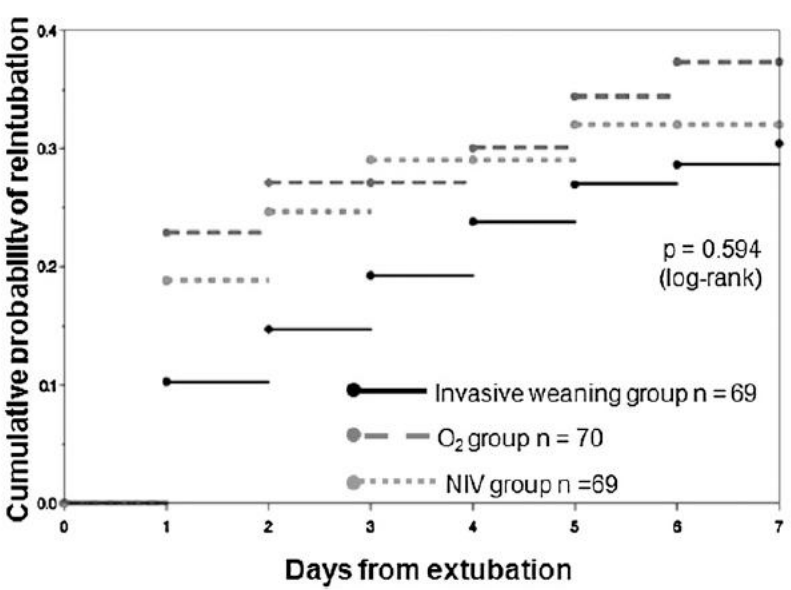
In conclusion, NIV permits earlier removal of the endotracheal tube than with conventional IPSV, and reduces the duration of daily ventilatory support without increasing the risk of weaning failures.

Noninvasive Ventilation and Weaning in Patients with Chronic Hypercapnic Respiratory Failure

A Randomized Multicenter Trial



Girault C, Am J Respir Crit Care Med 2011;184(6):672-679.



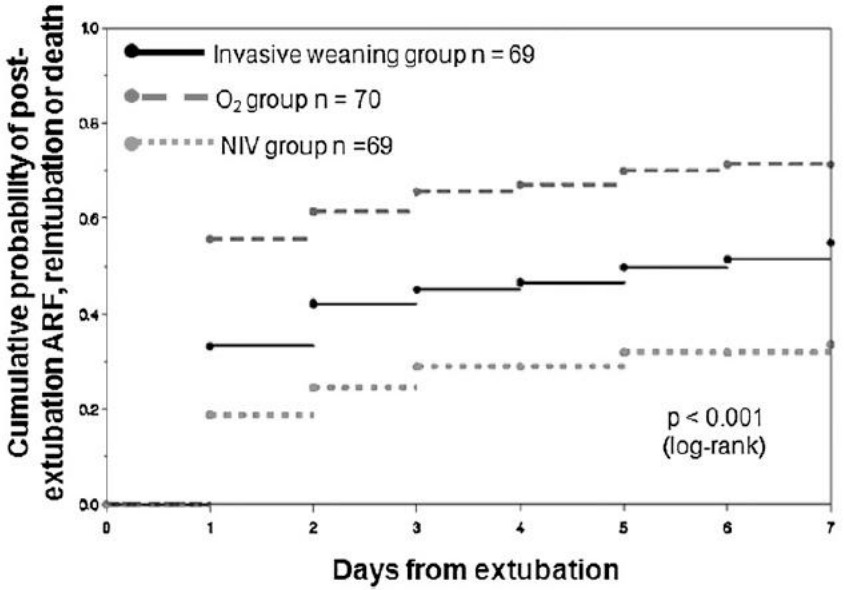


Figure 2. Probability of weaning failure within the first 7 days after extubation for the overall population according to study group. ARF = acute respiratory failure; NIV = noninvasive ventilation.

Conclusions: No difference was found in the reintubation rate between the three weaning strategies. NIV decreases the intubation duration and may improve the weaning results in difficult-to-wean patients with CHRF by reducing the risk of postextubation ARF. The benefit of rescue NIV in these patients deserves confirmation. Clinical trial registered with www.clinicaltrials.gov (NCT 00213499).

Girault C, Am J Respir Crit Care Med 2011;184(6):672-679.

Recommendations

- **We suggest NIV be used to facilitate weaning from mechanical ventilation in patients with hypercapnic respiratory failure.**

  (Conditional recommendation, moderate certainty of evidence.)

- We do not make any recommendation for hypoxaemic patients.

- **Should NIV be used in ARF following extubation from invasive mechanical ventilation?**

Table 9. Criteria Used to Separate Subjects Into High Risk and Low Risk for Re-Intubation

Mechanical Ventilation for at Least 12 h and at Least One of the Following	Low Risk	High Risk
Age 65 y	≤	>
APACHE II score of 12 at extubation	≤	>
BMI 30 kg/m_2	≤	>
Pulmonary Secretions	No problem	Problem
Comorbidities	≤1	>1
HF cause for mechanical ventilation	No	Yes
Moderate-severe COPD	No	Yes
Airway patency	No problem	Problem
Duration of mechanical venitlation	≤7 d	>7 d

Based on References 87 and 88.
APACHE = Acute Physiology and Chronic Health Evaluation
BMI = body mass index
HF = heart failure

Respir Care 2019;64(6):658–678.

Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

Effect of Postextubation High-Flow Nasal Cannula vs Conventional Oxygen Therapy on Reintubation in Low-Risk Patients

A Randomized Clinical Trial

JAMA. 2016 Apr 5;315(13):1354-61

Gonzalo Hernández, MD, PhD; Concepción Vaquero, MD; Paloma González, MD; Carles Subira, MD; Fernando Frutos-Vivar, MD; Gemma Rialp, MD; Cesar Laborda, MD; Laura Colinas, MD; Rafael Cuena, MD; Rafael Fernández, MD, PhD

JAMA | Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

Effect of Postextubation High-Flow Nasal Cannula vs Noninvasive Ventilation on Reintubation and Postextubation Respiratory Failure in High-Risk Patients

A Randomized Clinical Trial

JAMA. 2016 Oct 18;316(15):1565-1574.

Gonzalo Hernández, MD, PhD; Concepción Vaquero, MD; Laura Colinas, MD; Rafael Cuena, MD; Paloma González, MD; Alfonso Canabal, MD, PhD; Susana Sanchez, MD; Maria Luisa Rodriguez, MD; Ana Villasclaras, MD; Rafael Fernández, MD, PhD

Low risk

CONCLUSIONS AND RELEVANCE Among extubated patients at low risk for reintubation, the use of high-flow nasal cannula oxygen compared with conventional oxygen therapy reduced the risk of reintubation within 72 hours.

High risk

CONCLUSIONS AND RELEVANCE Among high-risk adults who have undergone extubation, high-flow conditioned oxygen therapy was not inferior to NIV for preventing reintubation and postextubation respiratory failure. High-flow conditioned oxygen therapy may offer advantages for these patients.

High-flow nasal cannula oxygen therapy decreases postextubation neuroventilatory drive and work of breathing in patients with chronic obstructive pulmonary disease

Table 3 Neuroventilatory drive and work of breathing parameters

	HFNC1	Conventional O_2	HFNC2
$EAdi_{PEAK}$ (μV)	15.4 ± 6.4	23.6 ± 10.5[a,b]	15.2 ± 6.4
$EAdi_{PTP}$ (μV/s)	13.7 ± 6.5	21.1 ± 11.8[a,b]	12.1 ± 5.2
$EAdi_{SLOPE}$	18.6 ± 6.5	24 ± 14.7[a,b]	17.6 ± 10.2
$PTP_{DI/b}$ (cmH_2O/s)	6.7 ± 2.7	9.9 ± 3.1[a,b]	6.7 ± 2.8
$PTP_{DI/min}$ (cmH_2O/s/min)	135 ± 60	211 ± 70[a,b]	132 ± 56

Data are expressed as mean ± standard deviation
Conventional O_2 conventional low flow oxygen therapy through a nonocclusive face mask, *$EAdi_{PEAK}$* diaphragm electrical activity peak, *$EAdi_{PTP}$* EAdi deflection inspiratory area, *$EAdi_{SLOPE}$* EAdi slope from the beginning of inspiration to $EAdi_{PEAK}$, *HFNC* high-flow nasal cannula oxygen therapy, *$PTP_{DI/b}$* inspiratory trans-diaphragmatic pressure-time product per breath, *$PTP_{DI/min}$* inspiratory trans-diaphragmatic pressure-time product per minute
[a] Different from HFNC1, ANOVA, with Bonferroni correction
[b] Different from HFNC2, ANOVA, with Bonferroni correction

Di mussi *et al. Critical Care* (2018) 22:180

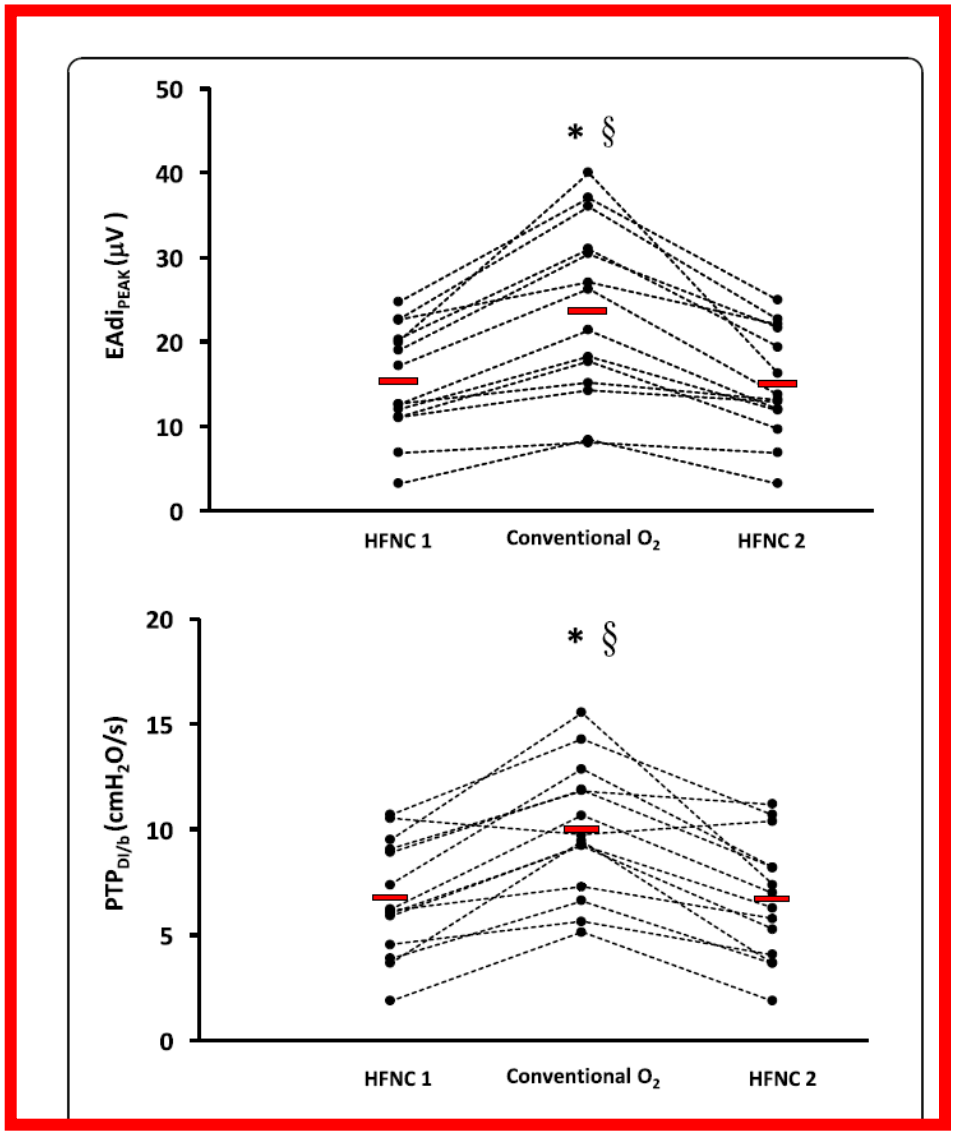


Fig. 4 Trend of the neuroventilatory drive, as expressed by the diaphragm electrical activity peak $EAdi_{PEAK}$, and of work of breathing, as expressed by the inspiratory P_{DI} pressure-time product per breath ($PTP_{DI/b}$) and per minute ($PTP_{DI/min}$). *Significant

Di mussi *et al. Critical Care* (2018) 22:180

Postextubation Recommendations

Risk for re-intubation	Recommendations
Low	**No indication**
High	
Need ventilatory assistance	**NIV**
***Hypoxemic need high PEEP**	**CPAP**
Hypoxemic doesn't need high PEEP	**HFNC**

***: (obese, abdominal surgery, significant atelectasis)**

Respir Care 2019;64(6):658–678.

Recommendations

- **We suggest that NIV be used to prevent post-extubation respiratory failure in high-risk patients post-extubation. (Conditional recommendation, low certainty of evidence.)**
- **We suggest that NIV should not be used to prevent post-extubation respiratory failure in non-high-risk patients. (Conditional recommendation, very low certainty of evidence.)**

Recommendation

- **We suggest that NIV should not be used in the treatment of patients with established post-extubation respiratory failure.**
- (Conditional recommendation, low certainty of evidence.)

2019台灣胸腔暨重症加護醫學會夏季會
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Should NIV be used in de novo ARF?

De novo respiratory failure

- **Respiratory failure occurring without prior chronic respiratory disease.**
- **Most patients are hypoxeamic respiratory failure**

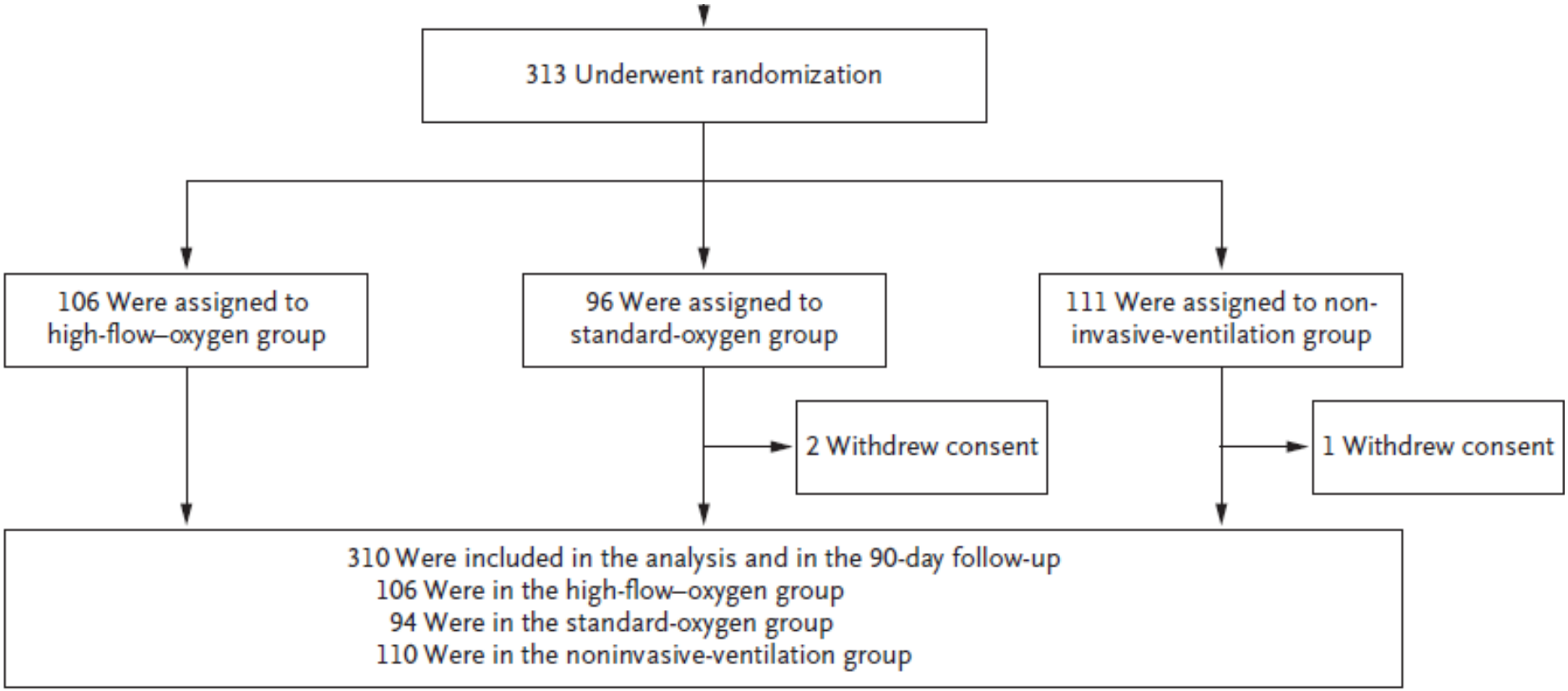
  -hypoxaemia (PaO2/FIO2 ⩽ 200)

  -tachypnea (RR >30 35 /min)
- **Nearly three quarters of the cases are pneumonia**
- **10-15% of patients with de novo acute respiratory failure or ARDS used NIV**

The NEW ENGLAND JOURNAL of MEDICINE

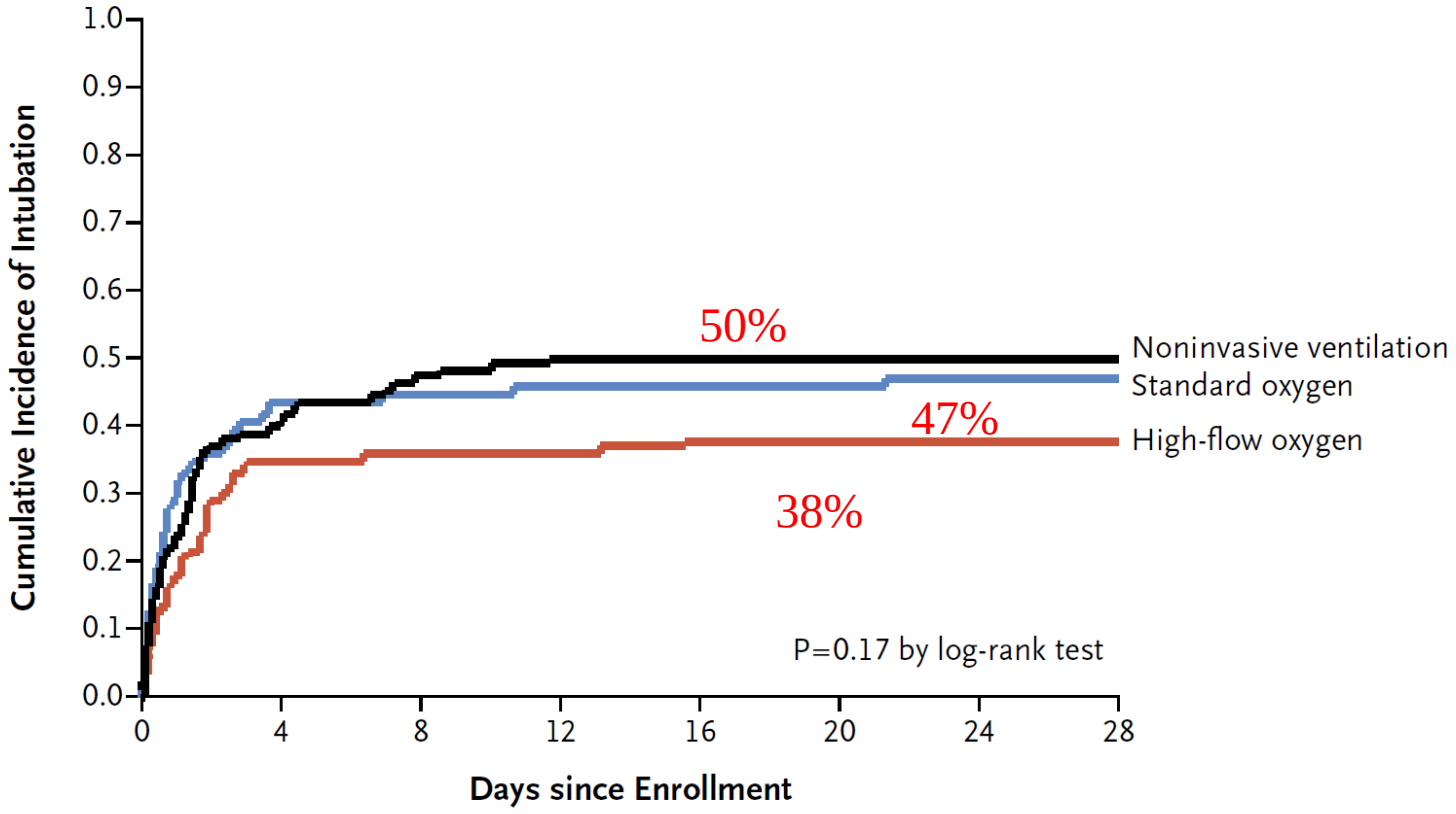
ORIGINAL ARTICLE

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



Intubation rate

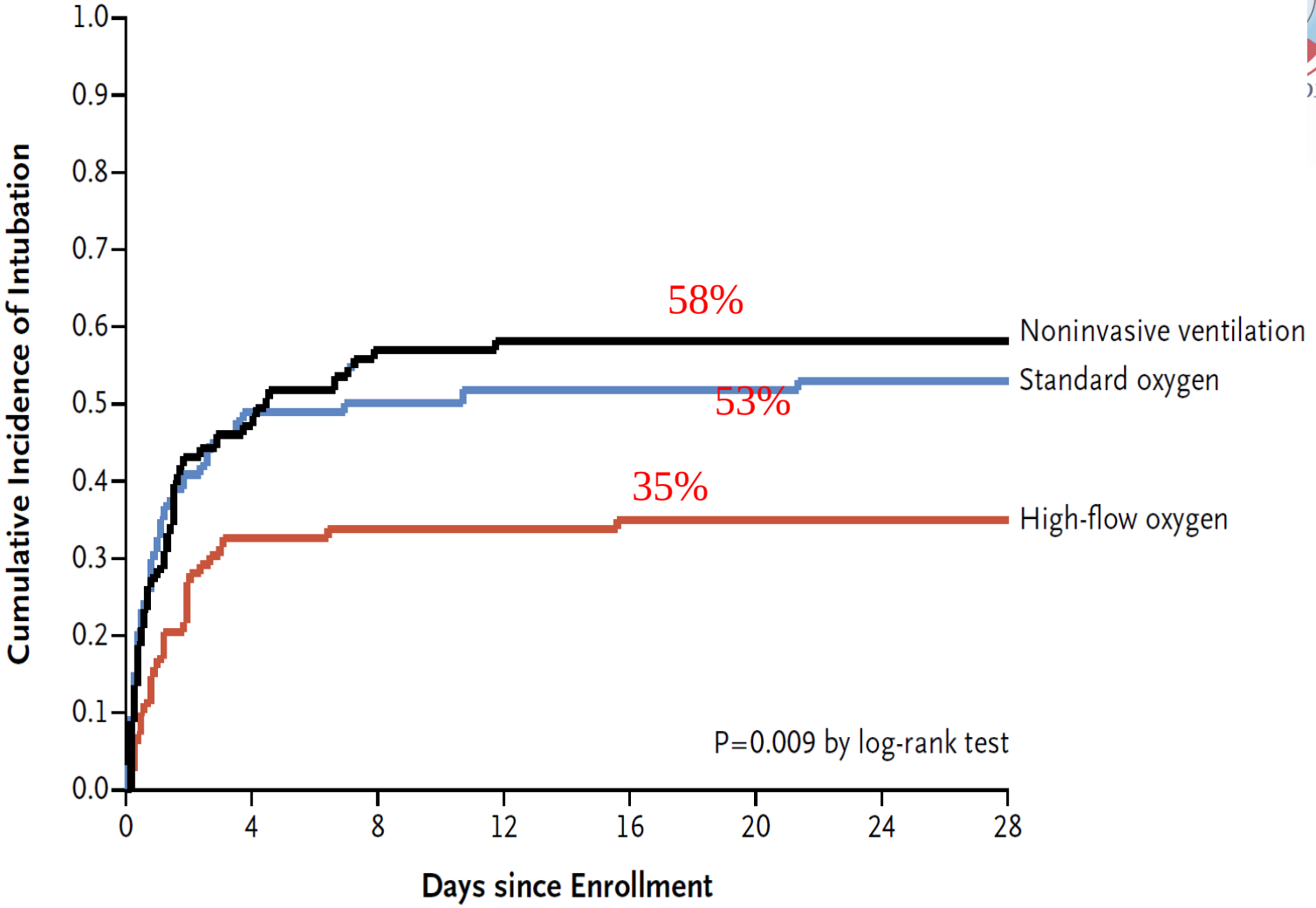
A **Overall Population**



No. at Risk

High-flow oxygen	106	68	67	67	65	65	65	65
Standard oxygen	94	52	50	49	49	49	48	48
Noninvasive ventilation	110	64	57	53	53	53	53	52

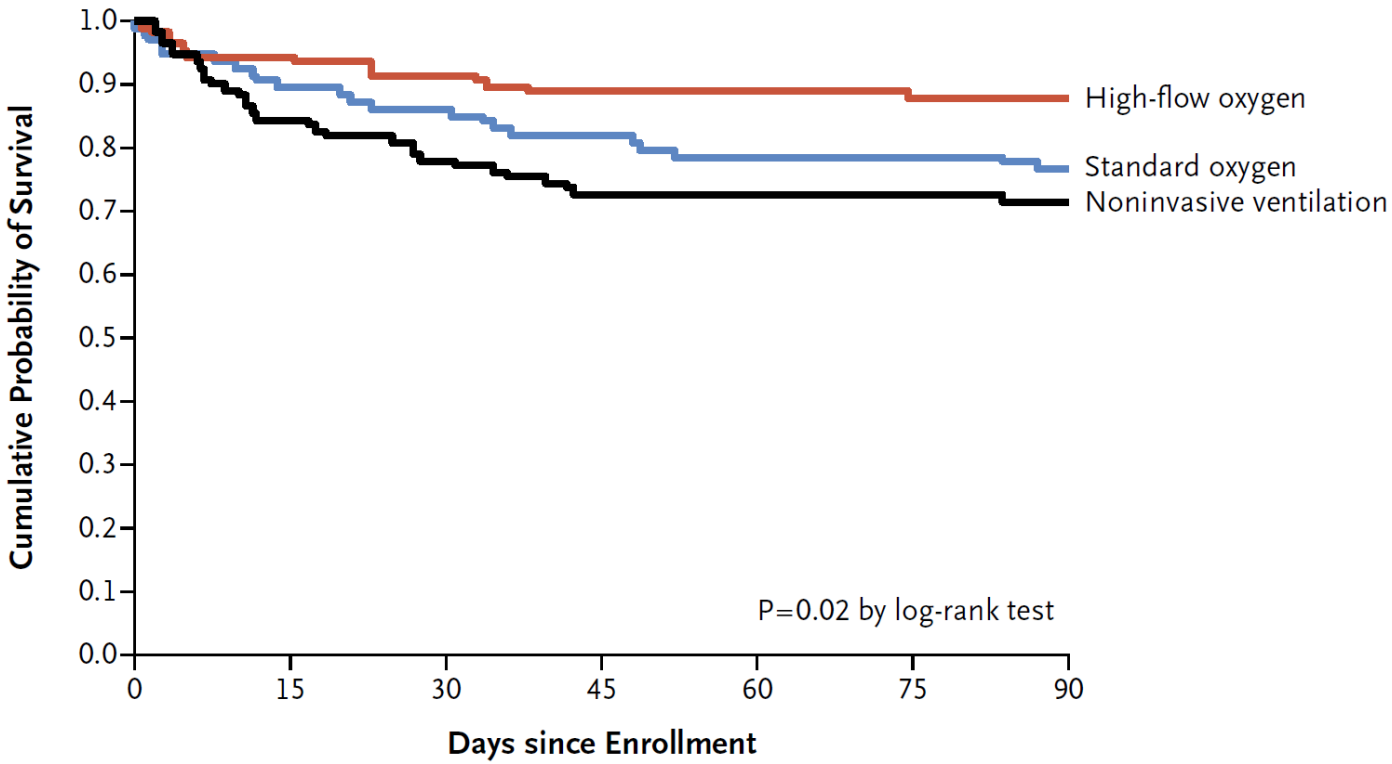
B Patients with a Pao_2:FIo_2 ≤200 mm Hg



No. at Risk

High-flow oxygen	83	55	54	54	53	53	53	53
Standard oxygen	74	37	35	34	34	34	33	33
Noninvasive ventilation	81	41	34	32	32	32	32	32

D90 Survival



No. at Risk							
High-flow oxygen	106	100	97	94	94	93	93
Standard oxygen	94	84	81	77	74	73	72
Noninvasive ventilation	110	93	86	80	79	78	77

Figure 3. Kaplan–Meier Plot of the Probability of Survival from Randomization to Day 90.

Predictors of Intubation in Patients With Acute Hypoxemic Respiratory Failure Treated With a Noninvasive Oxygenation Strategy*

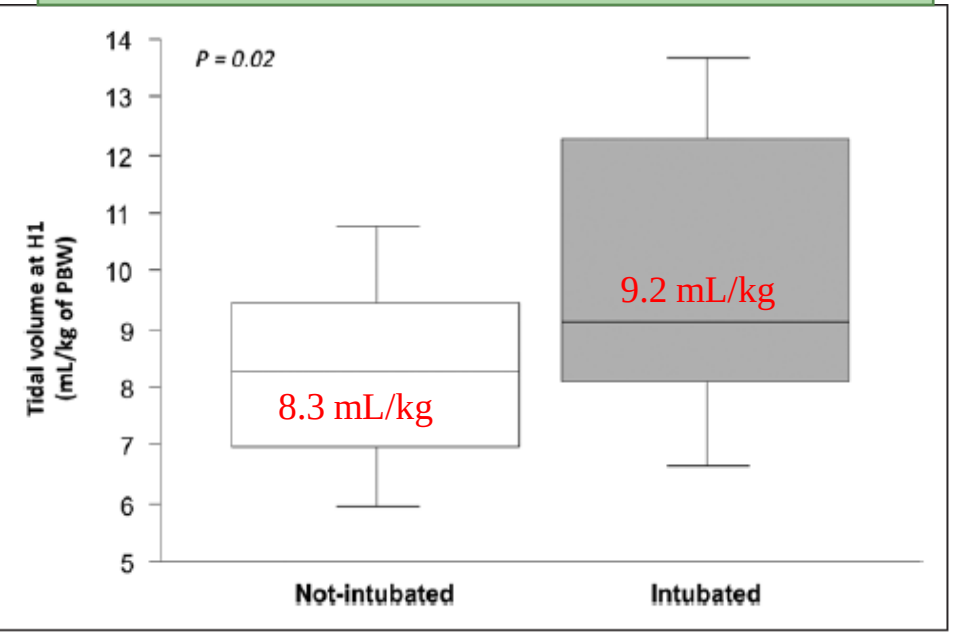
Jean-Pierre Frat, MD[1,2,3]; Stéphanie Ragot, PhD[4,5,6]; Rémi Coudroy, MD[1,2,3]; Jean-Michel Constantin, PhD[7]

TABLE 3. Multivariate Logistic Regression Analyses of Factors Associated With Intubation

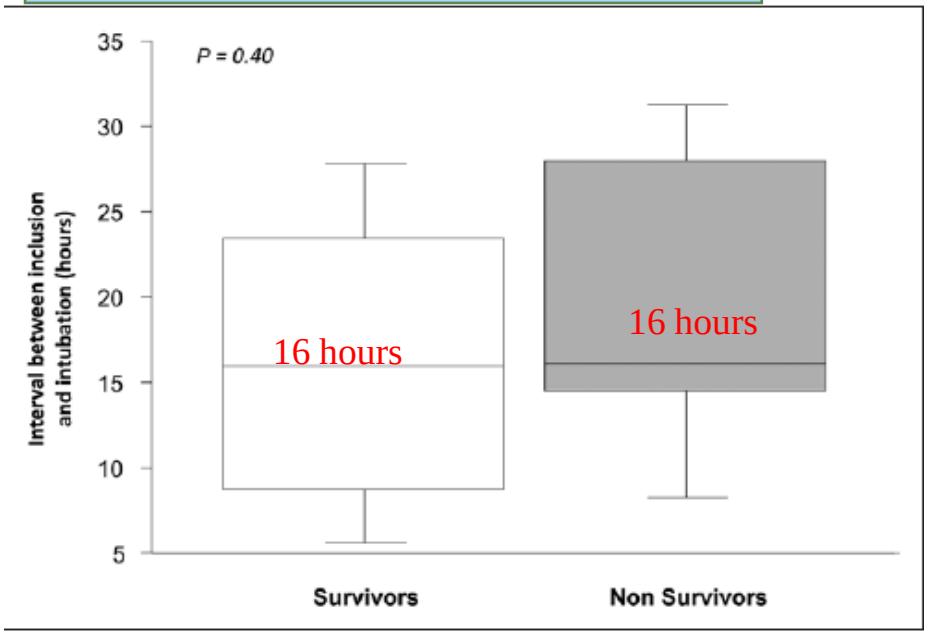
Risk Factors	OR (95% CI)	*p*
In patients treated with conventional O_2 therapy by nonrebreathing mask[a]		
Respiratory rate ≥ 30 breaths/min at H1	2.76 (1.13–6.75)	0.03
In patients treated with high-flow nasal cannula oxygen therapy[a]		
Heart rate at H1 (per beat/min)	1.03 (1.01–1.06)	< 0.01
In patients treated with noninvasive ventilation[ab]		
Tidal volume > 9 mL/kg of predicted body weight at H1	3.14 (1.22–8.06)	0.02
Pao_2/Fio_2 ≤ 200 mm Hg at H1	4.26 (1.62–11.16)	0.003

Crit Care Med 2018; 46:208–215

Tidal Volume



Interval before intubation



- ✓ **Predictors of intubation : TV>9 ml/Kg ; PF ratio < 200**
- ✓ **Poor outcomes were not because of delayed intubation**

ORIGINAL ARTICLE

Noninvasive Ventilation of Patients with Acute Respiratory Distress Syndrome

Insights from the LUNG SAFE Study

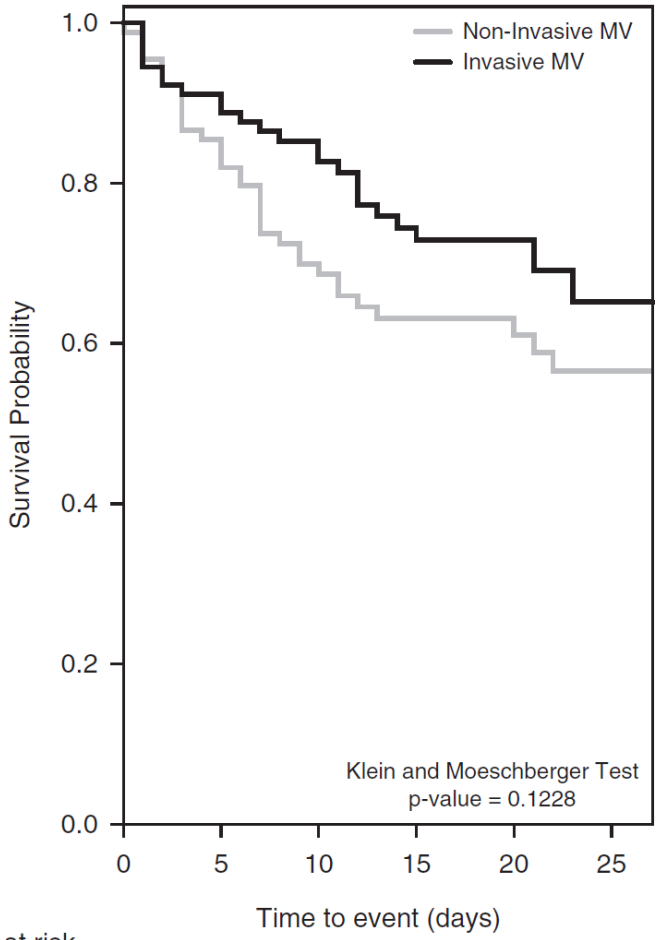
Giacomo Bellani[1,2], John G. Laffey[3,4,5,6,7,8], Tài Pham[9,10,11], Fabiana Madotto[12], Eddy Fan[8,13,14,15],

- NIV was used in 15% of ARDS patients
- NIV failure rate : 22.2% of mild, 42.3% of moderate, and 47.1% of severe ARDS

Am J Respir Crit Care Med 2017; 195

B

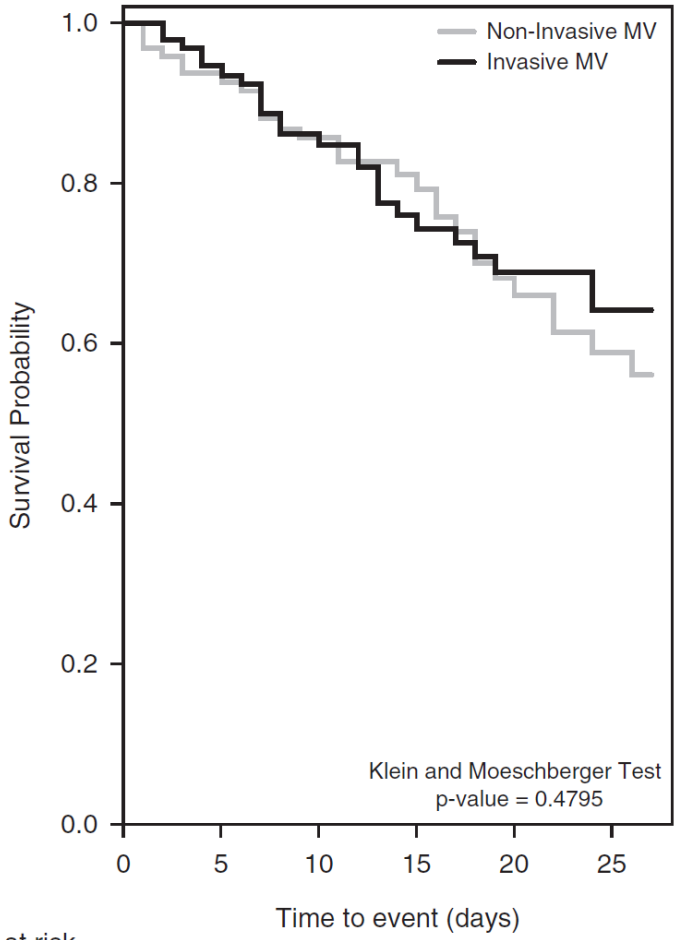
P/F ration <150mHg



# at risk						
Non-Invasive	90	73	55	39	30	21
Invasive	91	78	66	48	41	31

C

P/F ration >150mHg



# at risk						
Non-Invasive	97	86	64	47	31	23
Invasive	96	83	63	47	36	27

Higher ICU mortality in patients with a PaO2/FIO2 lower than 150 mm Hg received NIV than invasive-MV

Am J Respir Crit Care Med 2017; 195

Conclusion

- **NIV application is increasing in recent years**
- **The evidence is still not adequate to prove the effect of NIV on de novo respiratory failure**
- **Select suitable patients, suitable device**
- **Closely monitor, early detection of treatment failure**

Recommendation

- **Given the uncertainty of evidence we are unable to offer a recommendation on the use of NIV for de novo ARF.**

Take home message

- NIV should be managed by an experienced team
- Carefully selecte and avoid contraindications such as abnormal mental status, shock , upper airway obstruction, or too much secretions
- Closely monitored
- Reassessed early after starting NIV
- Intubated promptly if not improving

Thanks for your attention !