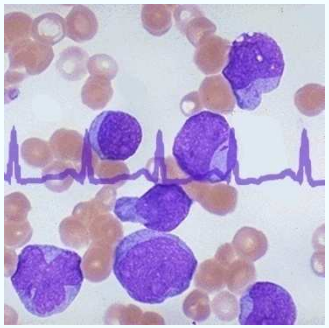
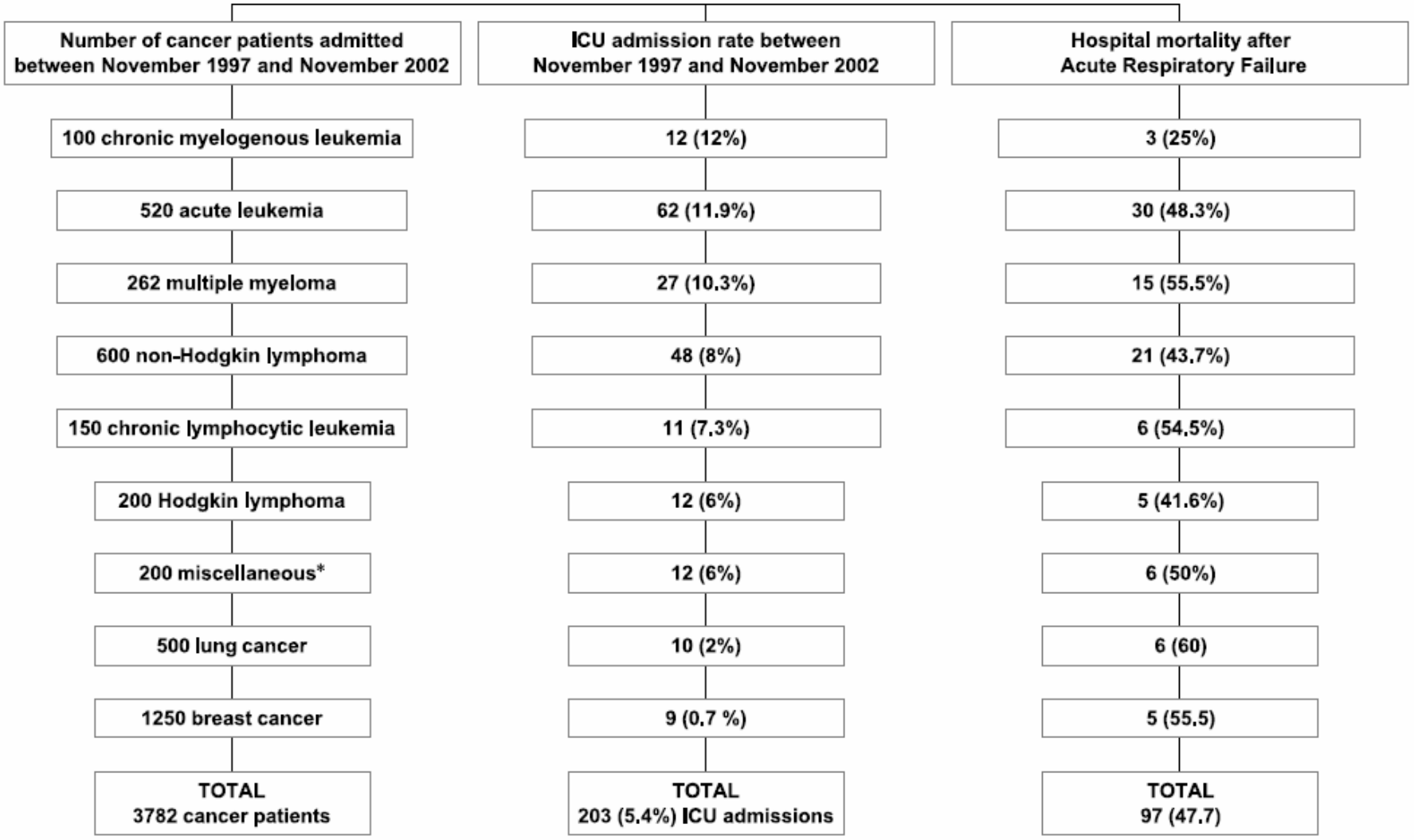
Ventilatory support in cancer patients



D. Benoit, MD, PhD

Department of Intensive Care Medicine
Ghent University Hospital

The Prognosis of Acute Respiratory Failure in Critically Ill Cancer Patients



Azoulay et al (*Medicine* 2004;83:360–370)

Case volume and mortality in haematological patients with acute respiratory failure

L. Lecuyer*,#,¶,+, S. Chevret*,#,¶,+, B. Guidet*,#,§, P. Aegerter*,#,f, P. Martel*,#,f, B. Schlemmer*,#,¶,+ and É. Azoulay*,#,¶,+

TABLE 2 Description of the study cohort according to year of intensive care unit admission

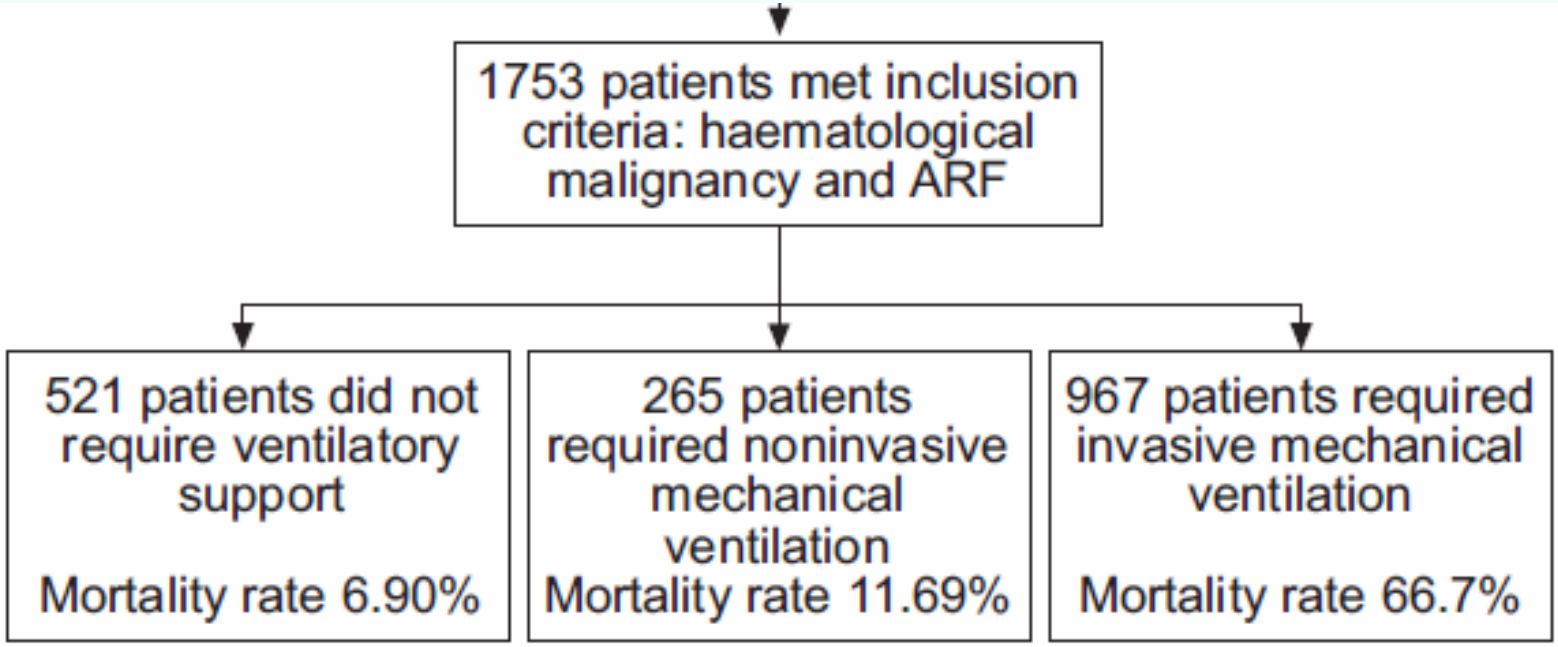
Year	ARF-H n	ARF-H-MV	Admissions from home	Neutropenia	Bone marrow transplant	Death %
1997	149	69 (46.30)	29 (19.46)	37 (24.83)	19 (12.75)	34.9
1998	196	92 (46.93)	46 (23.46)	56 (28.57)	26 (13.26)	35.2
1999	216	116 (53.70)	55 (25.46)	91 (42.12)	26 (12.03)	44.0
2000	207	100 (48.30)	51 (24.63)	83 (40.09)	20 (9.66)	37.3
2001	188	98 (52.12)	64 (34.04)	88 (42.51)	12 (6.38)	41.5
2002	223	125 (56.05)	61 (27.35)	81 (36.32)	14 (6.27)	44.4
2003	266	143 (53.75)	71 (26.69)	119 (44.73)	17 (6.39)	41.3
2004	308	224 (72.72)	98 (31.81)	18 (5.84)	23 (7.46)	42.5
Total	1753	967 (55.16)	475 (27.09)	573 (32.68)	157 (8.95)	712 (40.6)

Data are presented as n (%), unless otherwise stated. ARF-H: overall population of patients with acute respiratory failure and haematological malignancies; ARF-H-MV: subgroup of patients who required invasive mechanical ventilation.

Eur Respir J 2008; 32: 748–754

Case volume and mortality in haematological patients with acute respiratory failure

L. Lecuyer*,#,¶,+, S. Chevret*,#,¶,+, B. Guidet*,#,§, P. Aegerter*,#,f, P. Martel*,#,f, B. Schlemmer*,#,¶,+ and É. Azoulay*,#,¶,+



Eur Respir J 2008; 32: 748–754

La ventilation non-invasive (VNI) réduit le risque d'intubation et la mortalité chez le cancéreux avec une IRA

Oui

Non

La ventilation non-invasive (VNI) devrait être utiliser d'emblée chez le sujet cancéreux avec une IRA ne présentant pas de contre-indications classiques

Oui

Non

Invasive ……

or

…. non-invasive mechanical ventilation ?

…outside the clearcut indications for NIV :

Acute pulmonary edema

Acute COPD excacerbation

Invasive ……

or

…. non-invasive mechanical ventilation ?

Mortality in ventilated cancer patients

Author, year	Total n. of patients	Solid tumors	Haematol. Malign.	Hospital mort. (%)
Schuster, 1983	52	0	52	92
Ewer, 1986	46	46	0	91
Peters, 1988	116	0	116	82
Brunet, 1990	111	0	111	85
Sculier, 1991	64	30	27	80 / 70
Shapira, 1993	54	24	30	75 / 76
Epner, 1996	86	0	86	75
Groeger, 1999	782	305	404	63 / 84

Reluctance for ICU admission

« Patients who require mechanical ventilation longer than 24h are likely to die in the hospital (94% mortality in the largest study). Prognosis should be reassessed at frequent interval with particular attention to the developement of MOF »

Uptodate 2010

Mortality in ventilated cancer patients

Author, year	Total n. of patients	Solid tumors	Haematol. Malign.	Hospital mort. (%)
Kress, 1999	153	95	58	67
Massion, 2002	48	0	48	75
Benoit, 2003	88	0	88	68
Maschmeyer, 2003	189	103	86	73
Depuydt, 2004	166	0	166	71
Azoulay, 2004	203	23	180	75
Soares, 2005	463	359	104	65 / 68

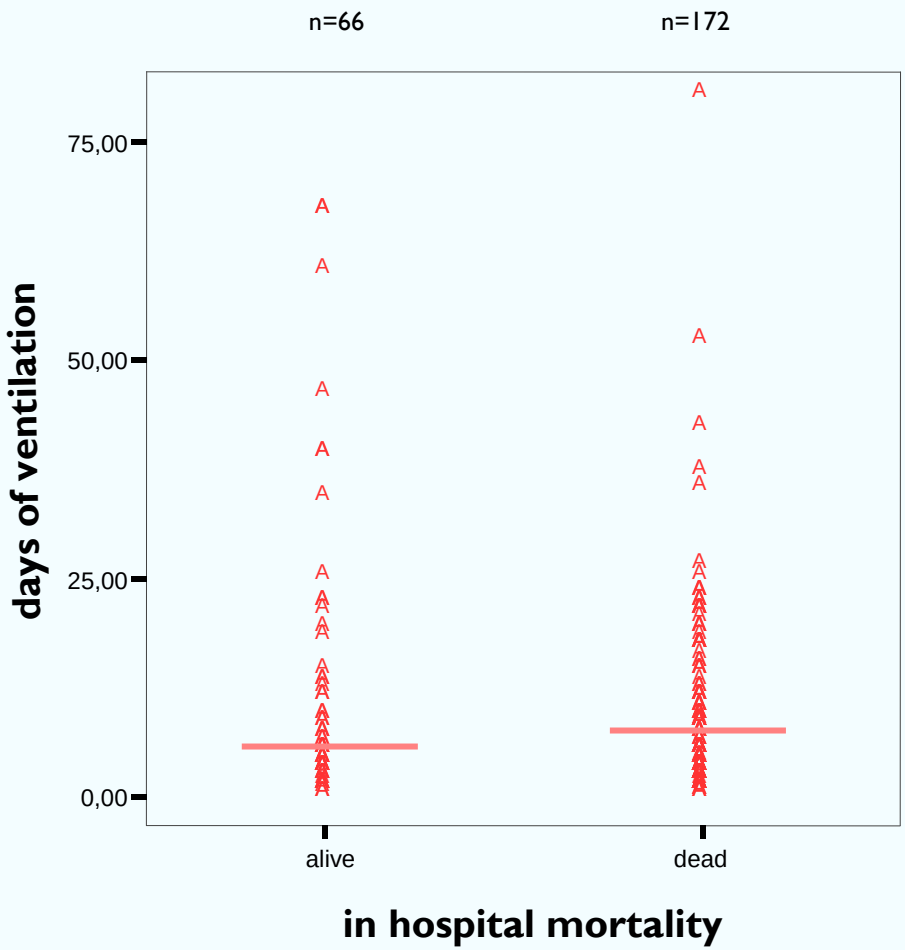
Duration of mechanical ventilation

100% mortality if duration of MV

> 5 days	Schuster, Am J Med 1983
> 6 days	Ewer, JAMA 1986
> 4 days*	Denardo, Crit Care Med 1989
> 7 days*	Torrecilla, Crit Care Med 1988
> 15 days*	Huaringa, Crit Care Med 2000
No restriction	> most experts in the field

* allo-BMT recipients

Duration of mechanical ventilation



P =0.94

Benoit, unpublished data 2005

Invasive ……

or

…. non-invasive mechanical ventilation ?

Noninvasive Ventilation for Treatment of Acute Respiratory Failure in Patients Undergoing Solid Organ Transplantation

A Randomized Trial

Massimo Antonelli, MD

Giorgio Conti, MD

Maurizio Bufi, MD

Maria Gabriella Costa, MD

Angela Lappa, MD

Monica Rocco, MD

Alessandro Gasparetto, MD

Gianfranco Umberto Meduri, MD

Context Noninvasive ventilation (NIV) has been associated with lower rates of endotracheal intubation in populations of patients with acute respiratory failure.

Objective To compare NIV with standard treatment using supplemental oxygen administration to avoid endotracheal intubation in recipients of solid organ transplantation with acute hypoxemic respiratory failure.

Design and Setting Prospective randomized study conducted at a 14-bed, general intensive care unit of a university hospital.

Patients Of 238 patients who underwent solid organ transplantation from December 1995 to October 1997, 51 were treated for acute respiratory failure. Of these, 40 were eligible and 20 were randomized to each group.

Intervention Noninvasive ventilation vs standard treatment with supplemental oxygen administration.

Main Outcome Measures The need for endotracheal intubation and mechanical ventilation at any time during the study, complications not present on admission, duration of ventilatory assistance, length of hospital stay, and intensive care unit mortality.

Results The 2 groups were similar at study entry. Within the first hour of treatment, 14 patients (70%) in the NIV group, and 5 patients (25%) in the standard treatment group improved their ratio of the PaO_2 to the fraction of inspired oxygen (FIO_2). Over time, a sustained improvement in PaO_2 to FIO_2 was noted in 12 patients (60%) in the NIV group, and in 5 patients (25%) randomized to standard treatment ($P = .03$). The use of NIV was associated with a significant reduction in the rate of endotracheal intubation (20% vs 70%; $P = .002$), rate of fatal complications (20% vs 50%; $P = .05$), length of stay in the intensive care unit by survivors (mean [SD] days, 5.5 [3] vs 9 [4]; $P = .03$), and intensive care unit mortality (20% vs 50%; $P = .05$). Hospital mortality did not differ.

Conclusions These results indicate that transplantation programs should consider NIV in the treatment of selected recipients of transplantation with acute respiratory failure.

JAMA. 2000;283:235-241 www.jama.com

-30%

IN THE PAST 2 DECADES, ADVANCEments in immunosuppressive strategies and major breakthroughs in surgical and organ preservation techniques have transformed organ transplantation into a therapy for an increasing population of patients with end-stage organ failure. Although preventing rejection remains the principle focus in improving overall survival statistics, pulmonary complications following transplantation are responsible for most morbidity and contribute substantially to the mortality associated with various organ transplantation procedures.[1] Approximately 5% of patients undergoing renal, hepatic, cardiac, or pulmonary transplantation develop pneumonia in the period after transplantation, which has

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.

ABSTRACT

Background Avoiding intubation is a major goal in the management of respiratory failure, particularly in immunosuppressed patients. Nevertheless, there are only limited data on the efficacy of noninvasive ventilation in these high-risk patients.

Methods We conducted a prospective, randomized trial of intermittent noninvasive ventilation, as compared with standard treatment with supplemental oxygen and no ventilatory support, in 52 immunosuppressed patients with pulmonary infiltrates, fever, and an early stage of hypoxemic acute respiratory failure. Periods of noninvasive ventilation delivered through a face mask were alternated every t[illegible]hours with periods of spontaneous breathing with s[illegible]plemental oxygen. The ventilation periods lasted [illegible]leas[illegible] 45 minutes. Decisions to intubate w[illegible]nade a[illegible]ord[illegible]ing to standard, predetermined criteria.

Results The base-line characteristics of the two groups were similar; each group of 26 patients included 15 patients with hematologic cancer and neutropenia. Fewer patients in the noninvasive-ventilation group than in the standard-treatment group required endotracheal intubation (12 vs. 20, P=0.03), had serious complications (13 vs. 21, P=0.02), died in the intensive care unit (10 vs. 18, P=0.03), or died in the hospital (13 vs. 21, P=0.02).

Conclusions In selected immunosuppressed patients with pneumonitis and acute respiratory failure, early initiation of noninvasive ventilation is associated with significant reductions in the rates of endotracheal intubation and serious complications and an improved likelihood of survival to hospital discharge. (N Engl J Med 2001;344:481-7.)

use of noninvasive ventilation at an early stage of hypoxemic acute respiratory failure would reduce the need for endotracheal intubation and the incidence of complications. In a prospective, randomized, controlled study, we compared the efficacy of noninvasive ventilation delivered intermittently through a face mask with that of standard medical treatment with supplemental oxygen and no ventilatory support in patients with immunosuppression from various causes in whom hypoxemic acute respiratory failure had been precipitated by pulmonary infiltrates and fever.

METHODS

S[illegible]dy De[illegible]n [illegible]nd Selection of Patients

[illegible]he experi[illegible]ental protocol was approved by the institutional r[illegible]w boa[illegible] [illegible] hospital, and all patients or the next of kin [illegible]vided [illegible]ritt[illegible] in[illegible]med consent. From May 1998 through December 1999, consecutive immunosuppressed patients who were transferred to our 16-bed intensive care unit and who had clinical manifestations of pulmonary infiltrates, fever, and hypoxemic acute respiratory failure were enrolled in the study. The immunosuppression could have been caused by neutropenia (defined as a polymorphonuclear leukocyte count of less than 1000 cells per cubic millimeter of blood) after chemotherapy or bone marrow transplantation in patients with hematologic cancers, drug-induced immunosuppression in organ-transplant recipients or as a result of corticosteroid or cytotoxic therapy for a nonmalignant disease, or the acquired immunodeficiency syndrome.

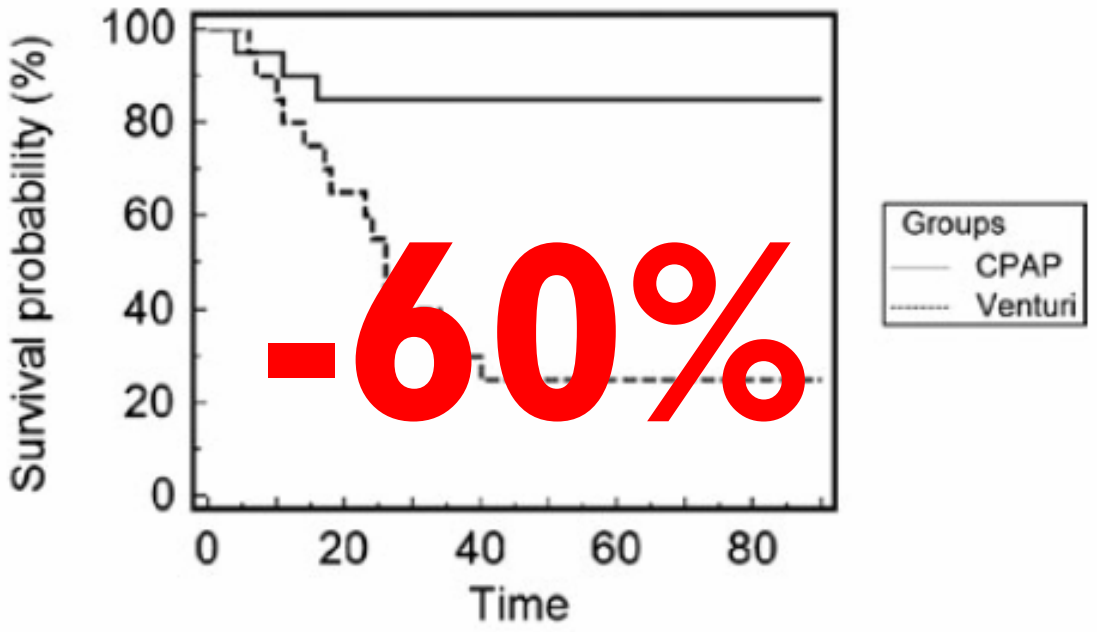
The criteria for eligibility were as follows: a clinical history of pulmonary infiltrates and fever, as evidenced by a temperature of more than 38.3°C, the finding of persistent pulmonary infiltrates on radiographs, and a deterioration in pulmonary gas exchange (leukocytosis and purulent tracheobronchial secretions were not required for enrollment, because most patients had hematologic cancers and neutropenia); severe dyspnea at rest; a respiratory rate of

Intensive Care Med (2010) 36:1666–1674
DOI 10.1007/s00134-010-1934-1

ORIGINAL

Vincenzo Squadrone
Massimo Massaia
Benedetto Bruno
Filippo Marmont
Michele Falda

Early CPAP prevents evolution of acute lung injury in patients with hematologic malignancy



Improved survival in cancer patients requiring mechanical ventilatory support: Impact of noninvasive mechanical ventilatory support

Elie Azoulay, MD; Corinne Alberti, MD; Caroline Bornstain, MD; Ghislaine Leleu, MD; Delphine Moreau, MD; Christian Recher, MD; Sylvie Chevret, MD, PhD; Jean-Roger Le Gall, MD; Laurent Brochard, MD, PhD; Benoît Schlemmer, MD

Table 3. Multivariable analysis: Additive predictors of 30-day mortality

Variables	Odds ratio	95% CI	*p* Value
Noninvasive mechanical ventilation	0.343	0.16–0.73	<.0001
ICU admission between 1996 and 1998	0.24	0.12–0.50	<.0001
SAPS II score (per point)	1.04	1.02–1.06	<.0001

(Crit Care Med 2001; 29:519–525)

The Prognosis of Acute Respiratory Failure in Critically Ill Cancer Patients

TABLE 6. Multivariable Analysis: Independent Predictors of Hospital Death*

	Odds Ratio	95% Confidence Interval	p Value
Cause of ARF			
Congestive heart failure	0.16	0.03–0.72	0.01
Invasive aspergillosis	3.78	1.05–14.24	0.049
No definite diagnosis	3.85	1.26–11.70	0.01
Need for vasopressors	3.19	1.28–7.95	0.01
Need for respiratory support			
NIMV only	1.58	0.37–6.70	0.52
NIMV followed by conventional MV	17.46	5.04–60.52	<0.0001
First-line conventional MV	8.75	2.35–32.54	0.001
Late NIMV failure†	10.64	1.05–107.83	0.04

*Hosmer-Lemeshow chi-square p value = 0.78.
†Late NIMV failure: need for conventional MV after 2 full days of NIMV.

Azoulay et al (*Medicine* 2004;83:360–370)

Case volume and mortality in haematological patients with acute respiratory failure

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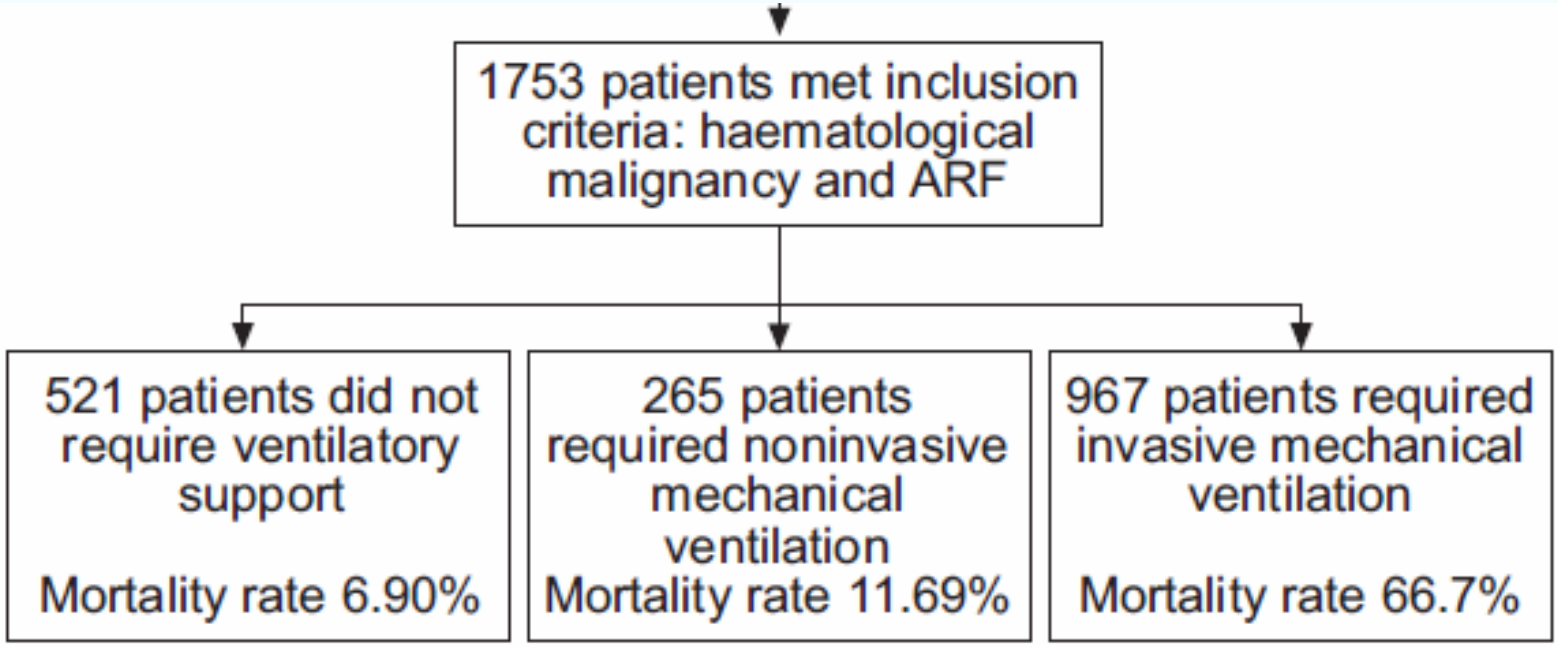

Eur Respir J 2008; 32: 748–754

Matched-cohort analysis (1:2)

Variables	NIV (n=26)	IMV (n=52)	P-value
age	44 (35-63)	58 (41-69)	0.06
AML	9 (35 %)	13 (25 %)	0.64
Active disease	7 (27 %)	12 (23 %)	0.78
Leukopenia	6 (23 %)	9 (17 %)	0.55
SAPS II	46	46	0.99
Pa02 / Fi02	72 (56-86)	147 (78-201)	<0.001
PEEP level	5 (5-8)	5 (5-10)	0.17
Vasopressor need	7 (27)	25 (48)	0. 09
Dialysis	4 (15)	18 (35)	0.08
Hospital mortality	17 (65 %)	34 (65 %)	0.99

Conditional logistic regression analysis: NIV OR 1.08; 95% CI, 0.34-3.38)

Depuydt, Chest 2004

The impact of the initial ventilatory strategy on survival in hematological patients with acute hypoxemic respiratory failure

Pieter O. Depuydt MD, PhD [a,*], Dominique D. Benoit MD, PhD [a], Carl D. Roosens MD [a], Fritz C. Offner MD, PhD [b], Lucien A. Noens MD, PhD [a], Johan M. Decruyenaere MD, PhD [a]

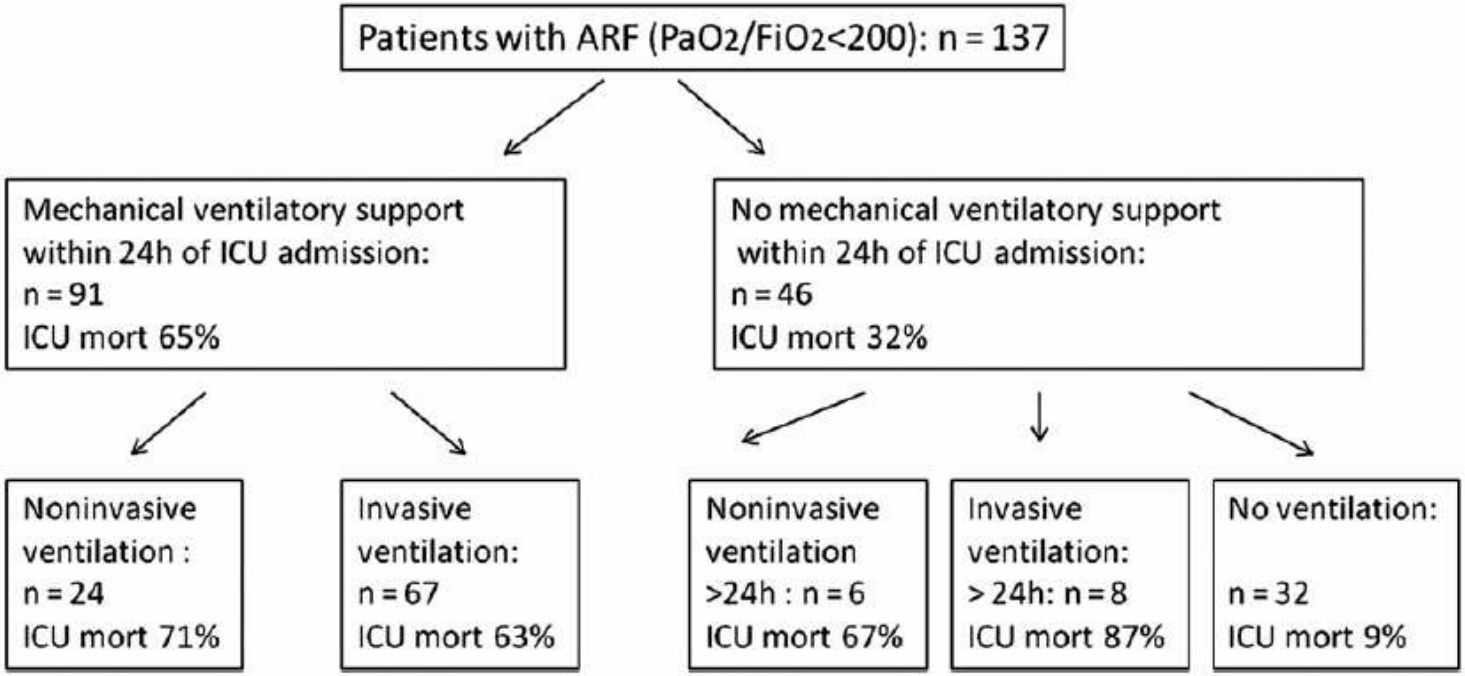

Fig. 1 Flow-chart of patients according to the ventilatory strategy.

Journal of Critical Care (2010) **25**, 30–36

The impact of the initial ventilatory strategy on survival in hematological patients with acute hypoxemic respiratory failure

Pieter O. Depuydt MD, PhD [a,*], Dominique D. Benoit MD, PhD [a], Carl D. Roosens MD [a], Fritz C. Offner MD, PhD [b], Lucien A. Noens MD, PhD [a], Johan M. Decruyenaere MD, PhD [a]

Multivariate, adjusted for organ failure and admission diagnosis [d]				
SOFA (per point)	0.27	1.31	1.11-1.55	.001
NIPPV within 24 h	0.62	1.85	0.49-6.93	.36
IPPV within 24 h	0.60	1.82	0.54-6.11	.33
Oxygen only within 24 h		1	Reference category	
Bacterial infection	−1.15	0.32	0.11-0.93	.04
Pulmonary disease	0.56	1.76	0.59-5.29	.31
Bilateral infiltrates	0.17	1.19	0.40-3.57	.76
Constant	−1.99	0.14		.05

Journal of Critical Care (2010) **25**, 30–36

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Hospital mortality	17 (65 %)	34 (65 %)	0.99

Too sick... too late..?

Conditional logistic regression analysis: NIV OR 1.08; 95% CI, 0.34-3.38)

Depuydt, Chest 2004

Variables	Alive (n=48)	Died (n=118)	P-value
Male gender	23 (48 %)	77 (65 %)	0.054
AML	8 (17 %)	36 (30 %)	0.08
Active disease	8 (17 %)	42 (35 %)	0.016
Leukopenia	7 (15 %)	38 (32 %)	0.02
SAPS II	50 ±14	62 ±19	<0.001
Intubation < 24 h	36 (75 %)	84 (72 %)	0.70
Non-invasive ventilation	9 (19 %)	17 (14 %)	0.25 *
PEEP level	5 (5-8)	5 (5-8)	0.76
Pa02 / Fi02	143 (67-274)	112 (76-206)	0.58
Bacteremia	13 (27 %)	16 (14 %)	0.04

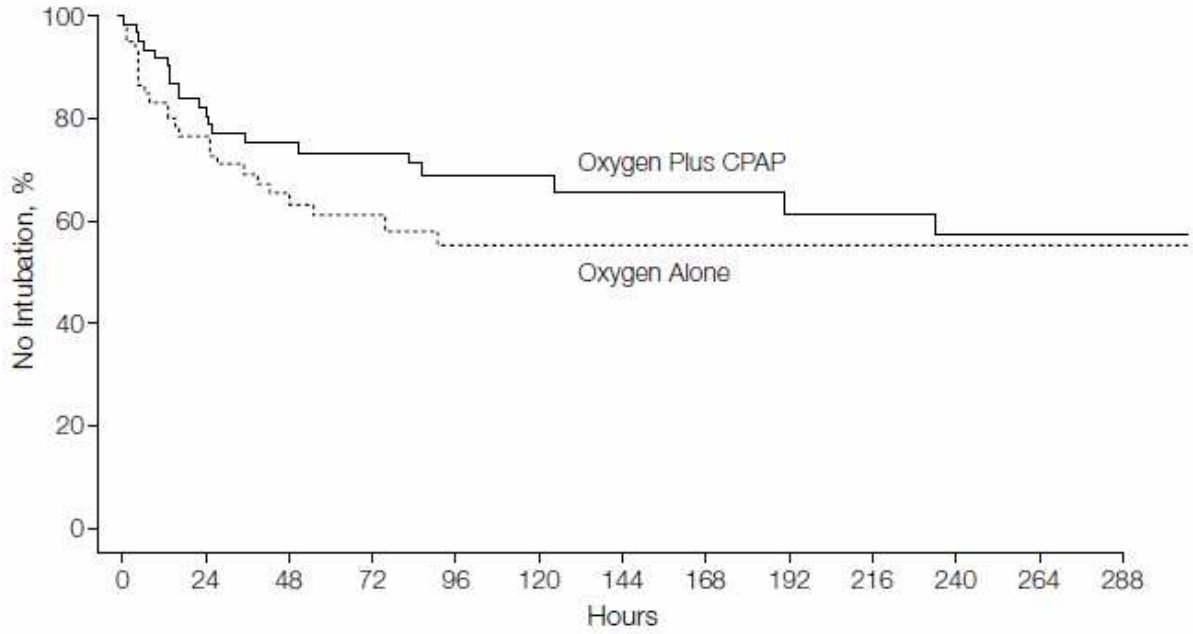
Depuydt, Chest 2004 — 26/166 (15.6 %)

Soares, Crit care Med 2005 — 40/463 (9.0 %)

Treatment of Acute Hypoxemic Nonhypercapnic Respiratory Insufficiency With Continuous Positive Airway Pressure Delivered by a Face Mask

A Randomized Controlled Trial

Figure 5. Time to Intubation in the 2 Randomization Groups



No. of Patients at Risk													
Oxygen Plus CPAP	62	47	38	33	25	20	19	17	17	15	13	12	9
Oxygen Alone	61	41	32	22	17	14	12	11	9	8	7	6	4

Non-invasive ventilation…

Start «early » …

NIV or IMV ?

1) Can the absolute risk reduction in mortality of 30% in the RCT's be attributed to the ventilation mode only ?

2) Explanation why non invasive mechanical ventilation is associated with a lower mortality ?

NIV or IMV ?

1) Can the absolute risk reduction in mortality of 30% in the RCTs be attributed to the ventilation mode only ?

Very small groups in a heterogeneous population

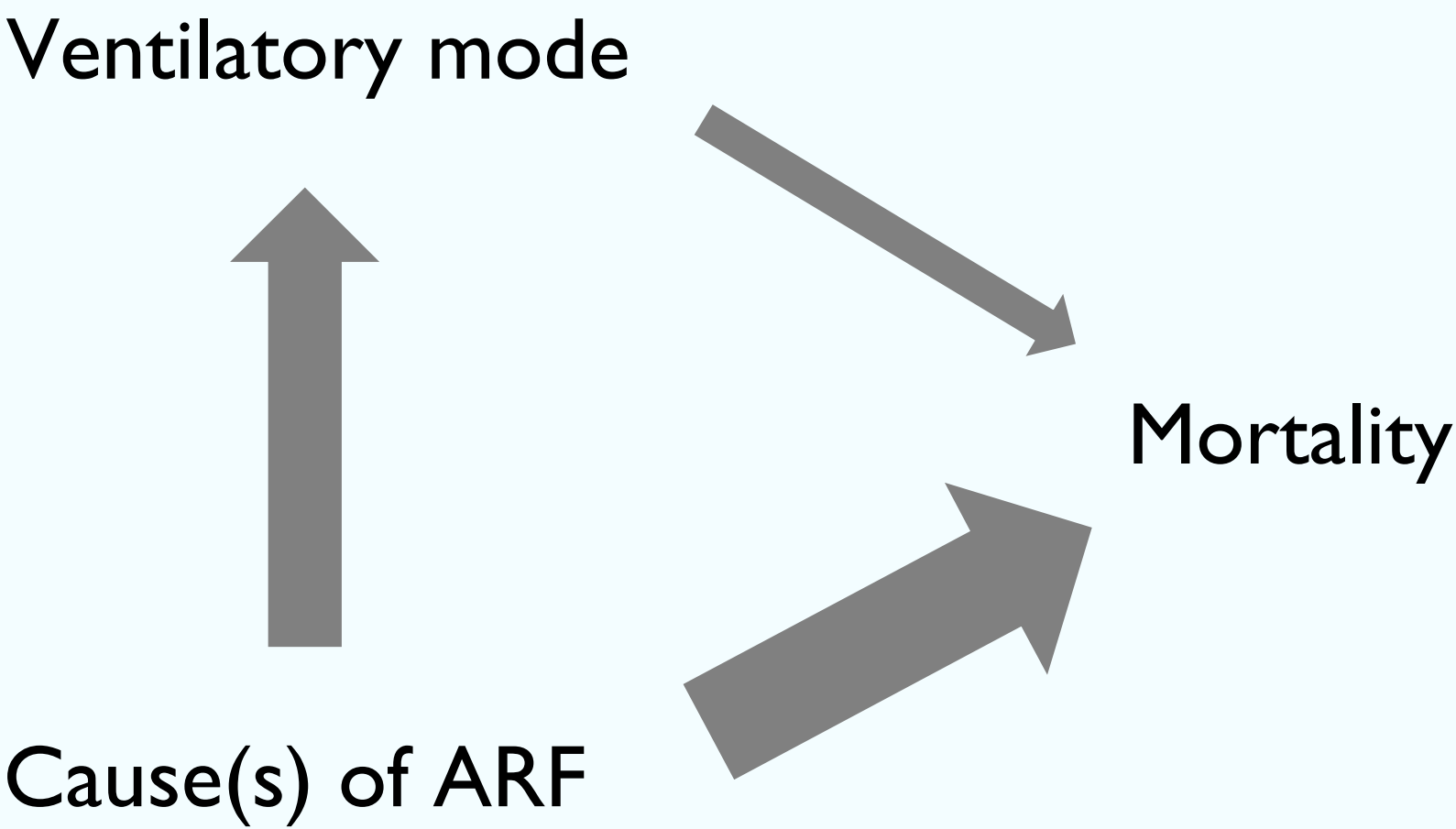
↓

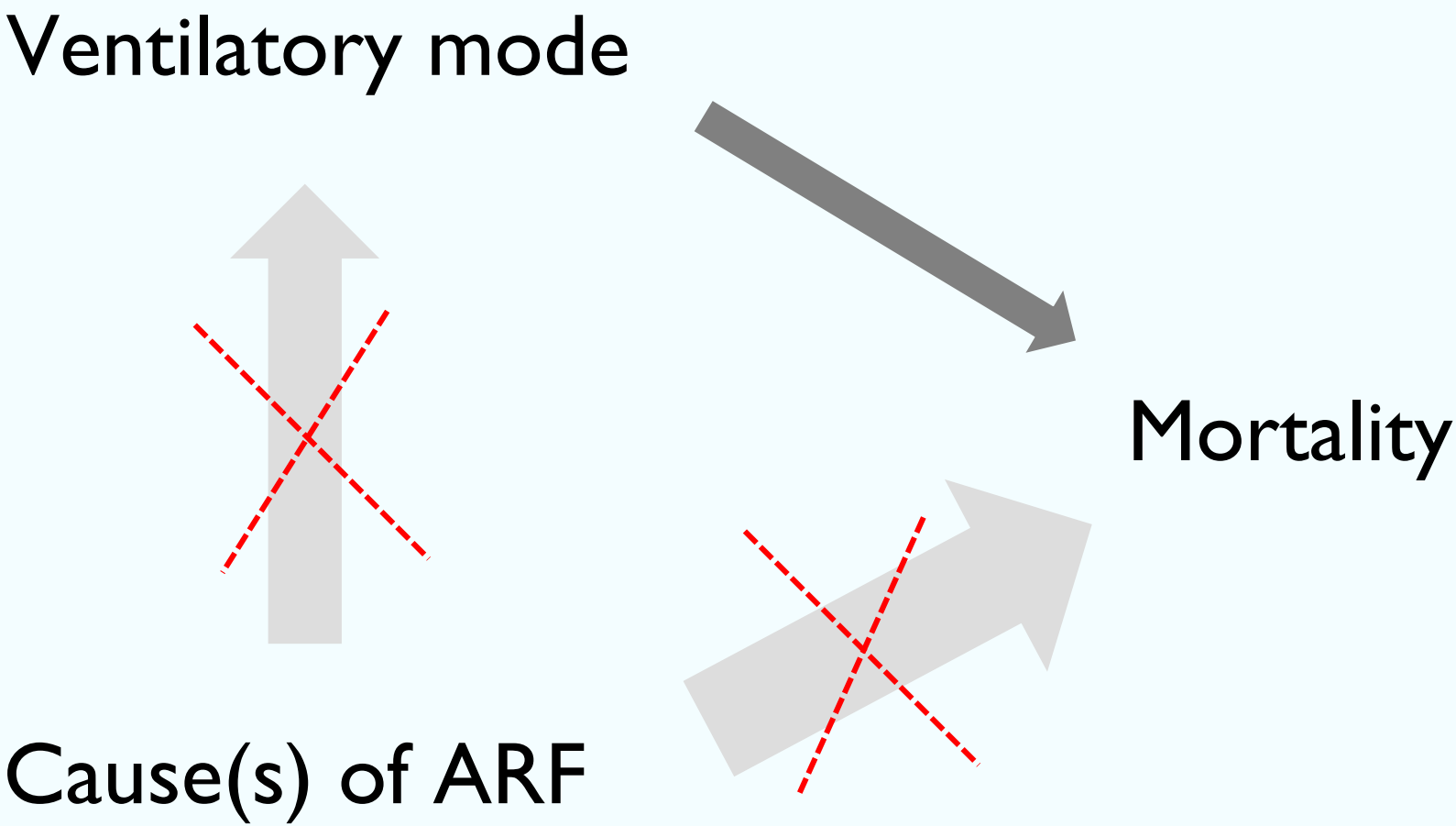
High probability of imbalances in baseline charactheristics

↓

Per definition not well randomized….

Study	Author	Journal	N	Mortality
Goal-directe therapy in severe sepsis and septic shock	Rivers N	NEJM 2001	263	30.5 % vs. 46.5 % (p=0.009)
Activated protein C Prowess trial (aPC)	Bernard	NEJM 2001	1728	24.7 % vs. 30.8 % (p=0.005)
ARDS network study low tidal volume	NIH	NEJM 2000	861	31 % vs. 39.8 % (p=0.007)
Low dose corticosteroids in septic shock	Annane	JAMA 2002	300	53 % vs. 63 % (p=0.02)
Tight glycemia control in the ICU	Van den Berghe	NEJM 2001	1548	4.6 % vs. 8 % (p=0.04)

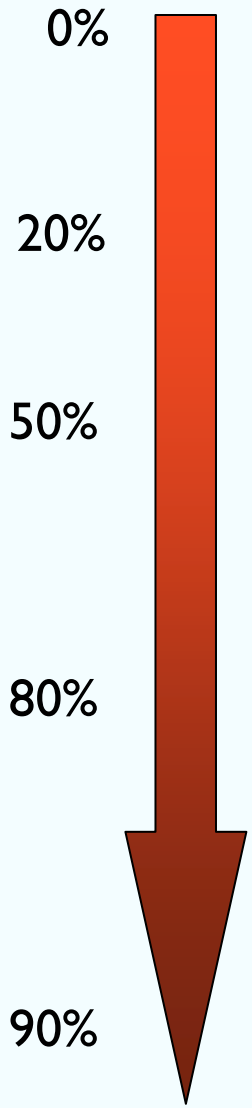

Ventilatory mode
Mortality
Cause(s) of ARF


Ventilatory mode
Mortality
Cause(s) of ARF

« Successful » NIV trial…

= surrogate marker for rapidly reversible and therefore per definition succesfull treatment of the underlying cause of ARF ?

Cause of ARF and mortality



I. Treatable and often rapidly reversible admission diagnosis

- Acute pulmonary edema
- COPD excacerbation

II. Treatable and potentially reversible admission diagnosis

- Documented or clinically suspected bacterial infection
- *Pneumocystis jerovicii* pneumonia

III. Difficult to treat and/or often slowly reversible admission diagnosis

- Invasion of hematological malignancy
- Viral pneumonia
- Invasive pulmonary aspergillosis

IV. Difficult to treat and often irreversible admission diagnosis

- No diagnosis, solid tumor invasion, idiopathic fibrosis…

Non-invasive ventilation…

Immunocompromised patients with respiratory failure (n=52)

	NIV (n=26)	Standard (n=26)	P-value
Final diagnosis	17 (65%)	11 (42%)	0.09
Intubation	12 (46%)	17 (77%)	0.03
ICU mortality	10 (38%)	18 (69%)	0.03
Hospital mortality	13 (50%)	21 (81%)	0.02

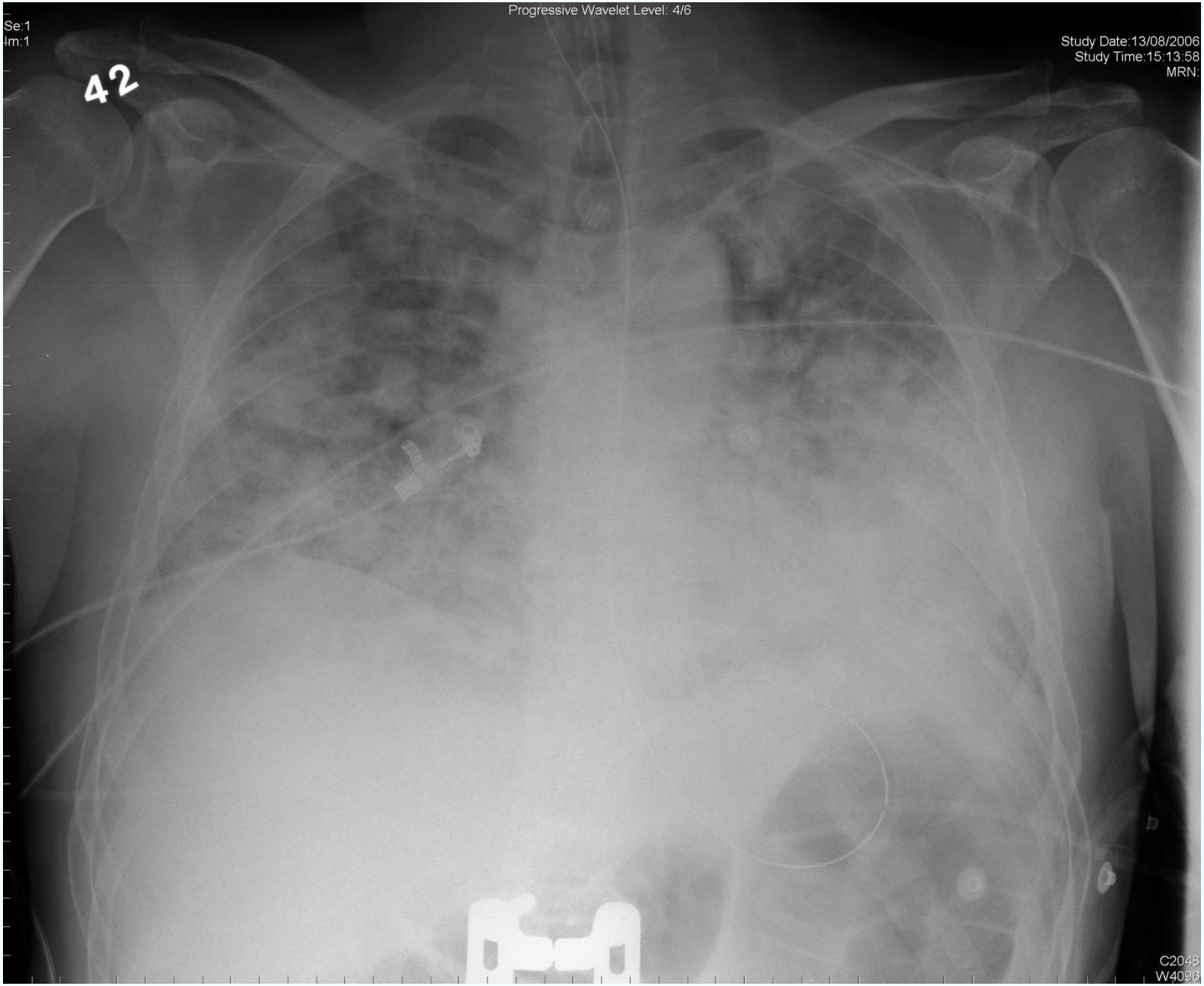
Hilbert, N Engl J Med 2001

Non-invasive ventilation…

Immunocompromised patients with respiratory failure (n=52)

	Final diagnosis (n=31)		No final diagnosis (n=21)	P-value
Bacteria	15	4 (26%)	-	
Bacteria + fungi	3	2 (67%)	-	
Fungi	7	2 (28%)	-	
CMV / PCP	6	4 (67%)	-	
ICU mortality	12 (38%)		16 (76%)	0.007
	4/15 (27%)		24/37 (65%)	0.01
	6/18 (30%)		22/34 (65%)	0.03

Hilbert, N Engl J Med 2001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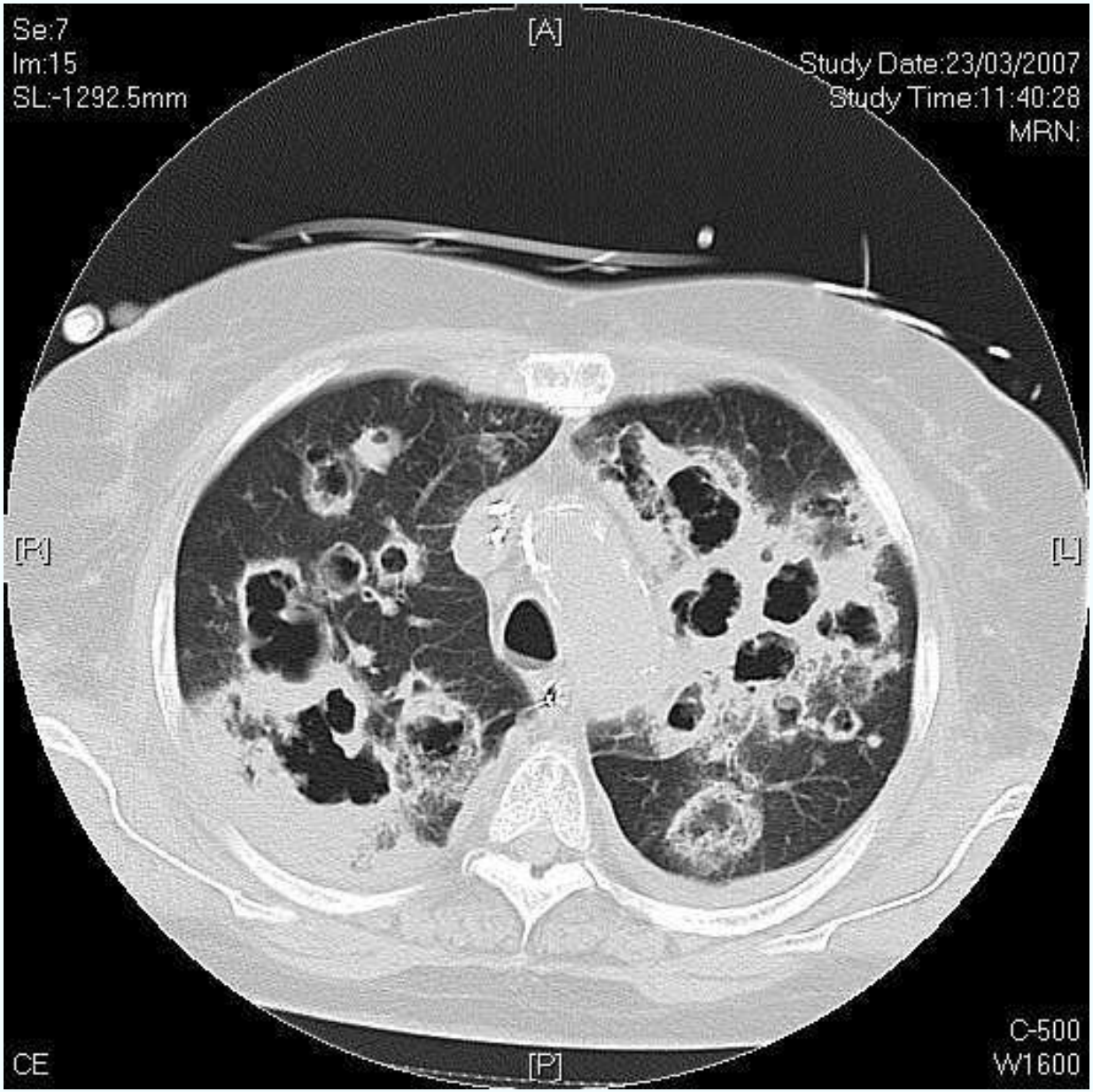
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Study Time:11:40:28
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Noninvasive vs Conventional Mechanical Ventilation in Acute Respiratory Failure

A Multicenter, Randomized Controlled Trial

Subgroup	NIMV intubation/N	CMV intubation/N	Relative risk for NIMV (95% CI)
Pneumonia	8/8	10/10	1 (indeterminate)
Acute exacerbation of COPD	5/11	7/7	0.40 (0.18 – 0.87)
Acute pulmonary edema	4/9	7/7	0.56 (0.32 – 1.00)
Other causes	1/3	9/9	0.33 (0.07 – 1.65)
With history of COPD	11/20	18/18	0.54 (0.36 – 0.82)
Without history of COPD	7/11	15/15	0.61 (0.37 – 1.01)
All patients	18/31	33/33	0.57 (0.42 – 0.78)

Teresa Honrubia, MD ***(CHEST 2005; 128:3916–3924)***

Noninvasive vs Conventional Mechanical Ventilation in Acute Respiratory Failure

A Multicenter, Randomized Controlled Trial

Subgroup	NIMV deaths/N	CMV deaths/N	Relative risk for NIMV (95% CI)
Pneumonia	4/8	8/10	0.53 (0.18 – 1.58)
Acute exacerbation of COPD	2/11	2/7	0.89 (0.06 – 13.7)
Acute pulmonary edema	1/9	1/7	1.00 (0.02 – 50.4)
Other causes	0/3	2/9	0.00 (indeterminate)
With history of COPD	3/20	7/18	0.40 (0.12 – 1.35)
Without history of COPD	4/11	6/15	0.74 (0.30 – 1.83)
All patients	7/31	13/33	0.53 (0.25 – 1.12)

Teresa Honrubia, MD (***CHEST 2005; 128:3916–3924***)

Noninvasive Ventilation for Treatment of Acute Respiratory Failure in Patients Undergoing Solid Organ Transplantation

A Randomized Trial

Table 2. Outcome Variables*

Variable	Noninvasive Ventilation Group (n = 20)	Standard Treatment Group (n = 20)	*P* Value
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

Noninvasive vs Conventional Mechanical Ventilation in Acute Respiratory Failure

A Multicenter, Randomized Controlled Trial

Subgroup	NIMV intubation/N	CMV intubation/N	Relative risk for NIMV (95% CI)
Pneumonia	8/8	10/10	1 (indeterminate)
Acute exacerbation of COPD	5/11	7/7	0.40 (0.18 – 0.87)
Acute pulmonary edema	4/9	7/7	0.56 (0.32 – 1.00)
Other causes	1/3	9/9	0.33 (0.07 – 1.65)
With history of COPD	11/20	18/18	0.54 (0.36 – 0.82)
Without history of COPD	7/11	15/15	0.61 (0.37 – 1.01)
All patients	18/31	33/33	0.57 (0.42 – 0.78)

Teresa Honrubia, MD ***(CHEST 2005; 128:3916–3924)***

Noninvasive vs Conventional Mechanical Ventilation in Acute Respiratory Failure

A Multicenter, Randomized Controlled Trial

Subgroup	NIMV deaths/N	CMV deaths/N	Relative risk for NIMV (95% CI)
Pneumonia	4/8	8/10	0.53 (0.18 – 1.58)
Acute exacerbation of COPD	2/11	2/7	0.89 (0.06 – 13.7)
Acute pulmonary edema	1/9	1/7	1.00 (0.02 – 50.4)
Other causes	0/3	2/9	0.00 (indeterminate)
With history of COPD	3/20	7/18	0.40 (0.12 – 1.35)
Without history of COPD	4/11	6/15	0.74 (0.30 – 1.83)
All patients	7/31	13/33	0.53 (0.25 – 1.12)

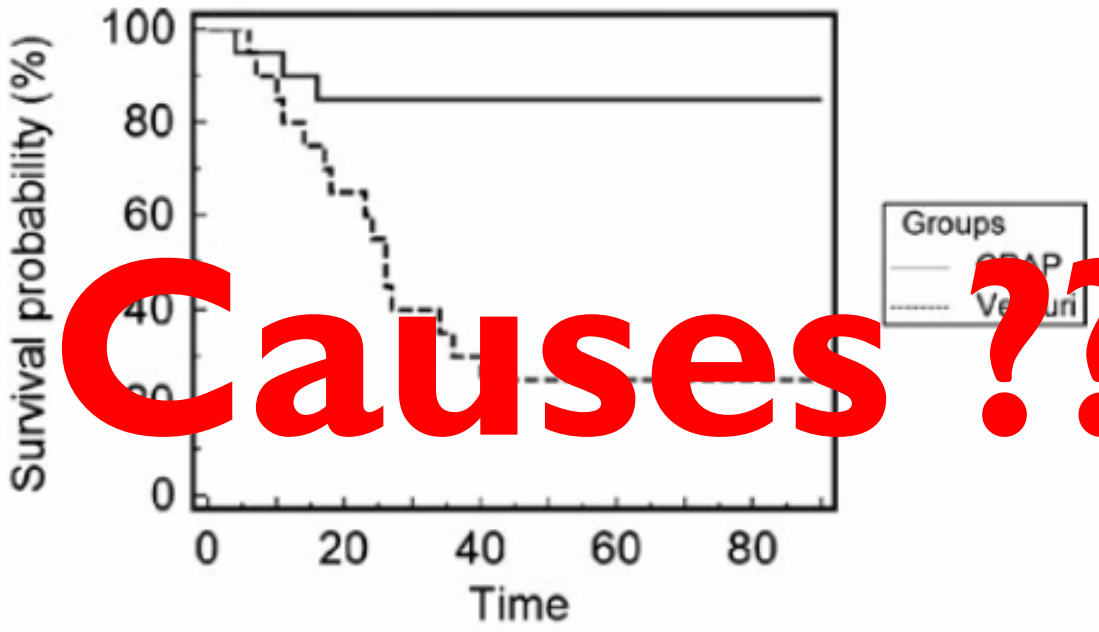
Teresa Honrubia, MD (***CHEST 2005; 128:3916–3924***)

Intensive Care Med (2010) 36:1666–1674
DOI 10.1007/s00134-010-1934-1

ORIGINAL

Vincenzo Squadrone
Massimo Massaia
Benedetto Bruno
Filippo Marmont
Michele Falda

Early CPAP prevents evolution of acute lung injury in patients with hematologic malignancy



Causes ??

Number at risk

Group: CPAP	20	19	17	17	17	17	17	17	17	17
Group: Venturi	20	17	13	8	5	5	5	5	5	5

NIV or IMV ?

1) Can the absolute risk reduction in mortality of 30% in the RCT's be attributed to the ventilation mode only ?

Very small groups in a heterogeneous population

Imbalances in baseline characteristics

No !!

Discrepancies with results in general ICU population

Only effective in well-known indications

Weaning protocol / short-acting drugs in IMV group ?

NIV or IMV ?

1) Can the absolute risk reduction in mortality of 30% in the RCT's be attributed to the ventilation mode only ?

No !!

2) Explanation why non invasive mechanical ventilation is associated with a lower mortality ?

Noninvasive Ventilation for Treatment of Acute Respiratory Failure in Patients Undergoing Solid Organ Transplantation

A Randomized Trial

Table 3. Serious Complications and Fatal Events in the 2 Groups

	Noninvasive Ventilation Group (n = 20)	Standard Treatment Group (n = 20)	*P* Value
No. (%) of patients with complications	8 (40)	12 (60)	.17
No. of complications occurring after intubation and causing death in intensive care unit	4	10	.05
No. of complications per patient	1.12	1.4	.60
Total No. of complications/No. causing death in intensive care unit (%)			
Cardiogenic shock	1/0 (5)	2/2 (10)	.50
Organ rejection	4/0 (20)	3/0 (15)	.25
Primary liver malfunction	1/0 (5)	1/0 (5)	.75
Worsening of infections present at study entry*	2/2 (10)	3/3 (15)	.50
Ventilator-associated pneumonia	2/2 (10)	4/4 (20)	.33
Severe sepsis and septic shock with multiple organ failure after study entry	4/4 (20)	10/8 (50)	.05
Gastrointestinal bleeding	1/0 (5)	0/0 (0)	.99

JAMA. 2000;283:235-241

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.

TABLE 3. SERIOUS COMPLICATIONS AND COMPLICATIONS RESULTING IN DEATH IN THE INTENSIVE CARE UNIT.*

VARIABLE	NONINVASIVE-VENTILATION GROUP (N=26)	STANDARD-TREATMENT GROUP (N=26)	P VALUE
Patients with serious complications — no. (%)	13 (50)	21 (81)	0.02
Patients with complications causing death in the ICU — no. (%)	10 (38)	18 (69)	0.03
Serious complications — no. causing death in the ICU/total no. (% of group)			
Severe sepsis or septic shock†	8/8 (31)	11/12 (46)	0.26
Cardiogenic shock	1/1 (4)	2/2 (8)	0.50
Renal failure‡	0/2 (8)	0/4 (15)	0.33
Hepatic failure‡	0/5 (19)	0/7 (27)	0.51
Ventilator-associated pneumonia§	2/2 (8)	6/6 (23)	0.12
Sinusitis	0/1 (4)	0/3 (12)	0.30
Gastrointestinal bleeding	0/1 (4)	1/2 (8)	0.50

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

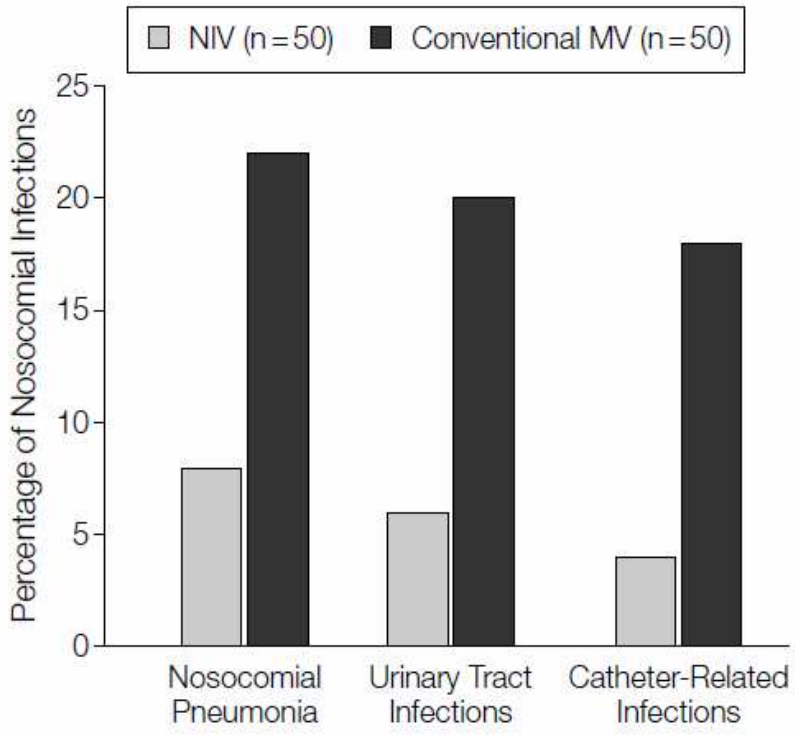
How many patients died directly because of nosocomial infection ….?

Did nosocomial infection indirectly increased mortality by increasing the duration of ventilation ?

Time of onset ….?

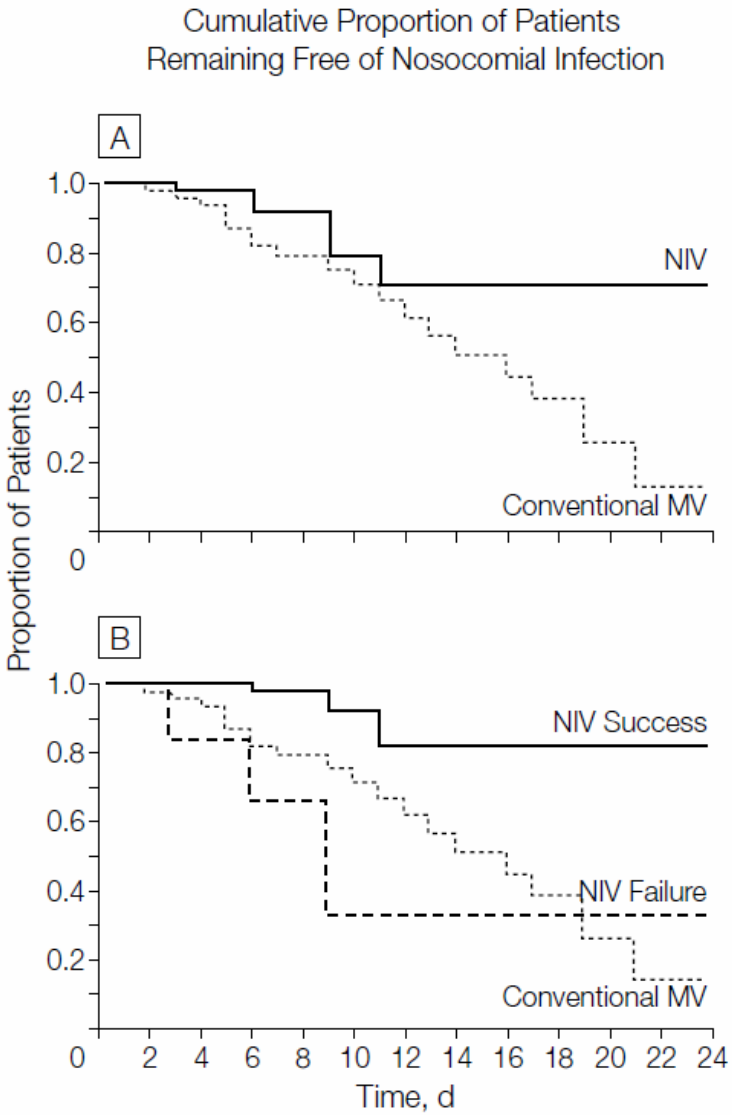
Association of Noninvasive Ventilation With Nosocomial Infections and Survival in Critically Ill Patients

Figure 2. Frequency of Nosocomial Infections in the 2 Groups



Emmanuelle Girou, PharmD *JAMA. 2000;284:2361-2367*

Figure 3. Kaplan-Meier Curves for Nosocomial Infection



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No !!

2) Explanation why non invasive mechanical ventilation is associated with a lower mortality ?

?

Does noninvasive positive pressure ventilation improve outcome in acute hypoxemic respiratory failure? A systematic review

Sean P. Keenan, MD, FRCPC, MSc (Epid); Tasnim Sinuff, MD, FRCPC; Deborah J. Cook, MD, FRCPC, MSc (Epid); Nicholas S. Hill, MD

Context: The results of studies on noninvasive positive pressure ventilation (NPPV) for acute hypoxemic respiratory failure unrelated to cardiogenic pulmonary edema have been inconsistent.

Objective: To assess the effect of NPPV on the rate of endotracheal intubation, intensive care unit and hospital length of stay, and mortality for patients with acute hypoxemic respiratory failure not due to cardiogenic pulmonary edema.

Data Source: We searched the databases of MEDLINE (1980 to October 2003) and EMBASE (1990 to October 2003). Additional data sources included the Cochrane Library, personal files, abstract proceedings, reference lists of selected articles, and expert contact.

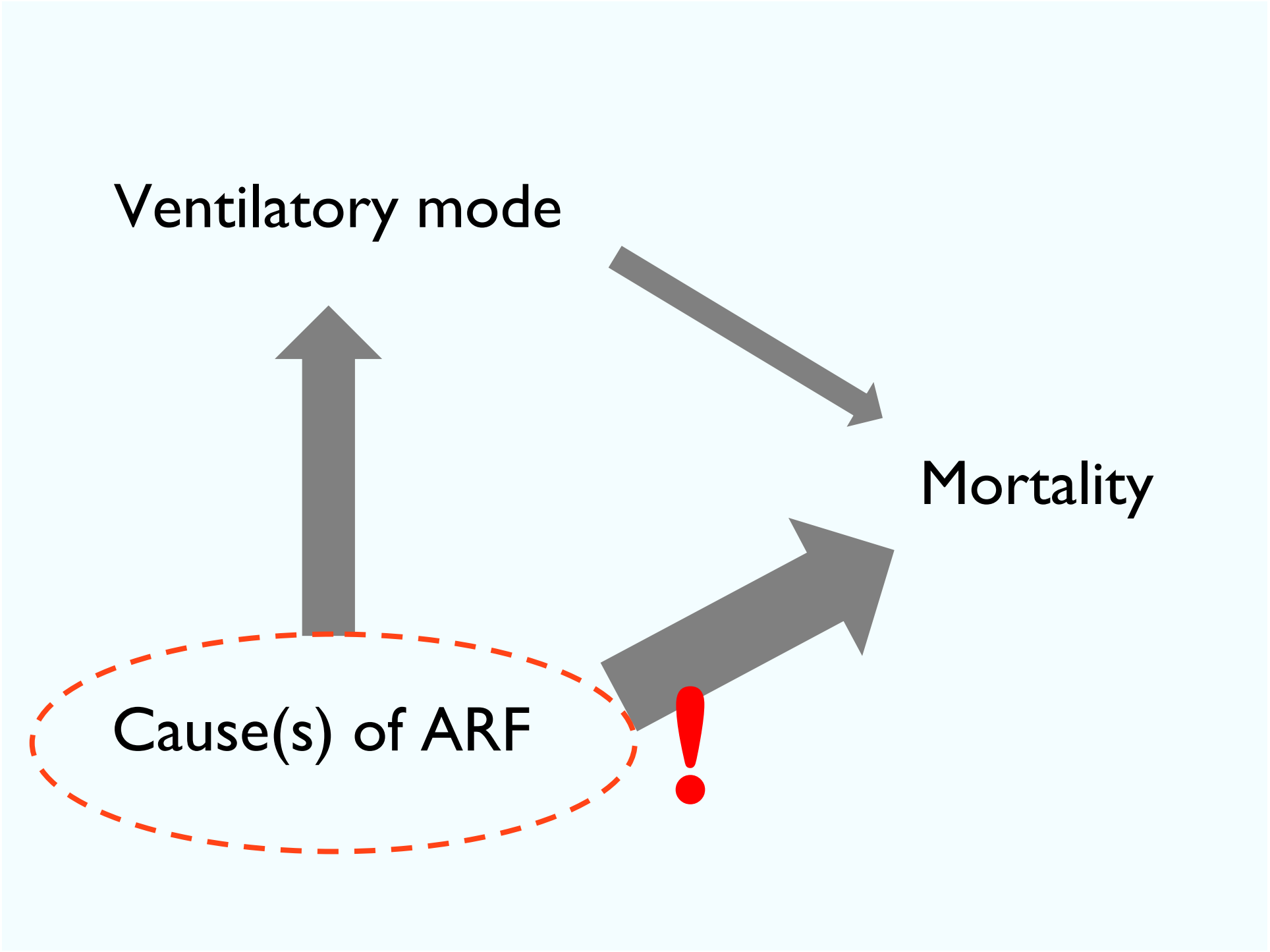
Study Selection: We included studies if a) the design was a randomized controlled trial; b) patients had acute hypoxemic respiratory failure not due to cardiogenic pulmonary edema; c) the interventions compared noninvasive ventilation and standard therapy with standard therapy alone; and d) outcomes included need for endotracheal intubation, length of intensive care unit or hospital stay, or intensive care unit or hospital survival.

Data Extraction: In duplicate and independently, we abstracted data to evaluate methodological quality and results.

Data Synthesis: The addition of NPPV to standard care in the setting of acute hypoxemic respiratory failure reduced the rate of endotracheal intubation (absolute risk reduction 23%, 95% confidence interval 10–35%), ICU length of stay (absolute reduction 2 days, 95% confidence interval 1–3 days), and ICU mortality (absolute risk reduction 17%, 95% confidence interval 8–26%). However, trial results were significantly heterogeneous.

Conclusion: Randomized trials suggest that patients with acute hypoxemic respiratory failure are less likely to require endotracheal intubation when NPPV is added to standard therapy. However, the effect on mortality is less clear, and the heterogeneity found among studies suggests that effectiveness varies among different populations. As a result, the literature does not support the routine use of NPPV in all patients with acute hypoxemic respiratory failure. (Crit Care Med 2004; 32:2516–2523)

KEY WORDS: noninvasive positive pressure ventilation; acute hypoxemic respiratory failure; cardiogenic pulmonary edema; hospital length of stay; hospital mortality


Ventilatory mode
Mortality
Cause(s) of ARF
!

The Prognosis of Acute Respiratory Failure in Critically Ill Cancer Patients

TABLE 5. Predictors of Failure of Noninvasive Mechanical Ventilation (NIMV)

	Odds Ratio	95% Confidence Interval	p Value
Diagnosis of the malignancy <30 days	2.15	1.08–4.30	0.02
Pulmonary involvement by the malignancy	3.20	1.18–8.67	0.02
Symptom duration at ARF onset (per additional day)	0.93	0.87–0.99	0.04
ARDS	3.08	1.45–6.61	0.003
Steroid therapy	2.39	1.21–4.70	0.001
Duration of NIMV (per additional day)	1.44	1.22–1.69	<0.0001
No definite etiologic diagnosis of the ARF	2.43	1.02–2.79	0.04
Need for vasopressors	3.20	1.54–6.65	0.001

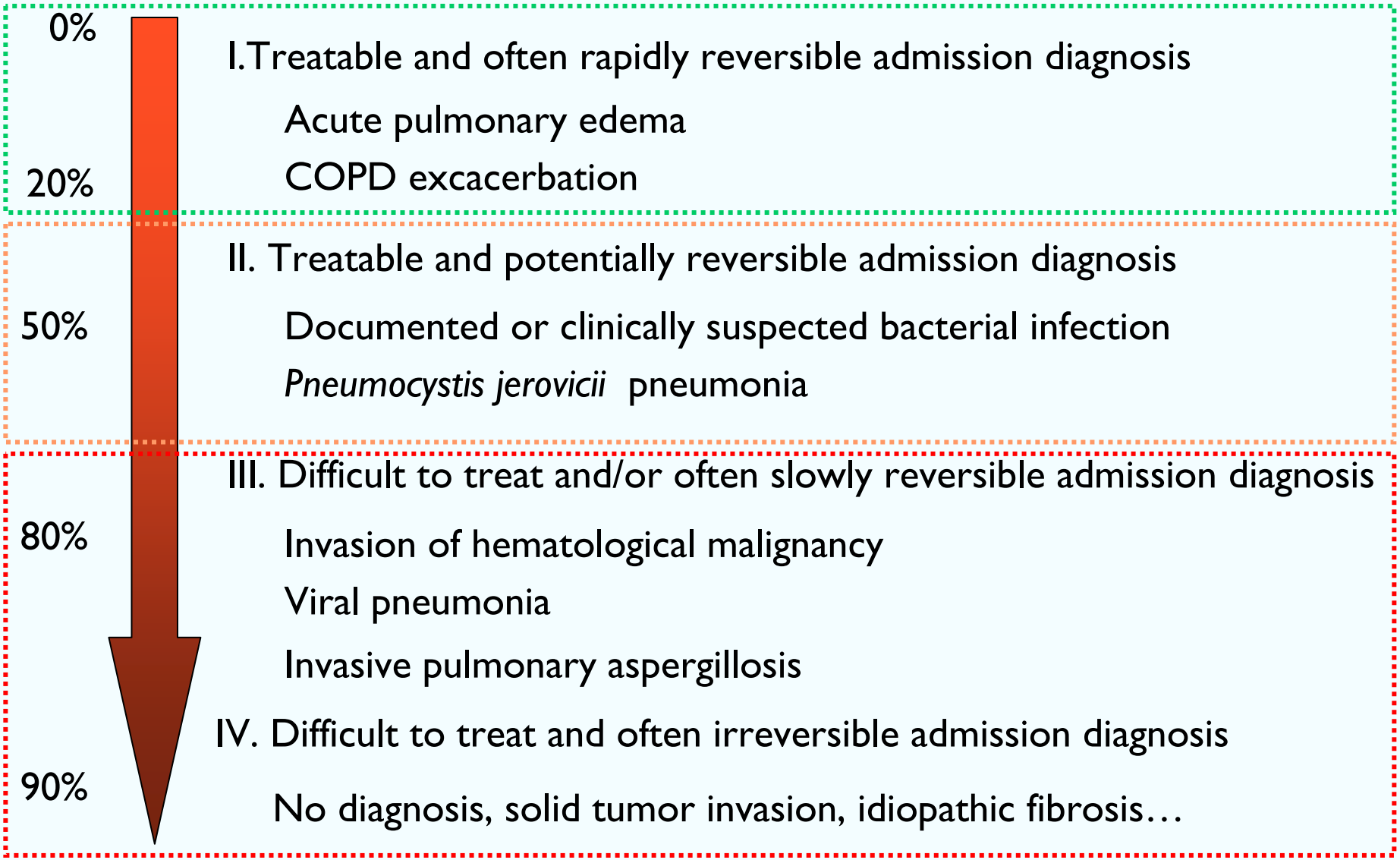
TABLE 6. Multivariable Analysis: Independent Predictors of Hospital Death*

	Odds Ratio	95% Confidence Interval	p Value
Cause of ARF			
Congestive heart failure	0.16	0.03–0.72	0.01
Invasive aspergillosis	3.78	1.05–14.24	0.049
No definite diagnosis	3.85	1.26–11.70	0.01
Need for vasopressors	3.19	1.28–7.95	0.01
Need for respiratory support			
NIMV only	1.58	0.37–6.70	0.52
NIMV followed by conventional MV	17.46	5.04–60.52	<0.0001
First-line conventional MV	8.75	2.35–32.54	0.001
Late NIMV failure†	10.64	1.05–107.83	0.04

*Hosmer-Lemeshow chi-square p value = 0.78.
†Late NIMV failure: need for conventional MV after 2 full days of NIMV.

Azoulay et al (*Medicine* 2004;83:360–370)

Admission diagnosis and mortality



Non-invasive ventilation…

Start « early » …

… for a potentially rapidly reversible complication…

NIV or IMV ?

NIV trial: for how long ?

The Prognosis of Acute Respiratory Failure in Critically Ill Cancer Patients

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Azoulay et al (*Medicine* 2004;83:360–370)

Outcome in Noninvasively and Invasively Ventilated Hematologic Patients With Acute Respiratory Failure*

Pieter O. Depuydt, MD; Dominique D. Benoit, MD; Koenraad H. Vandewoude, MD; Johan M. Decruyenaere, MD, PhD; and Francis A. Colardyn, MD

Table 3—*Results From Stepwise Logistic Regression Procedure

Variable	Parameter Estimate	OR	95% CI	p Value
Female sex	−1.01	0.36	0.16–0.82	0.014
Intubation < 24 h	−1.25	0.29	0.11–0.78	0.015
Bacteremia < 48 h	−1.52	0.22	0.08–0.61	0.003
AML	1.004	2.73	1.05–7.11	0.04
SAPS II	0.08	1.07	1.04–1.11	< 0.001

(CHEST 2004; 126:1299–1306)

Predictors of noninvasive ventilation failure in patients with hematologic malignancy and acute respiratory failure*

Mélanie Adda, MD; Isaline Coquet, MD; Michaël Darmon, MD; Guillaume Thiery, MD; Benoît Schlemmer, MD; Élie Azoulay, MD, PhD

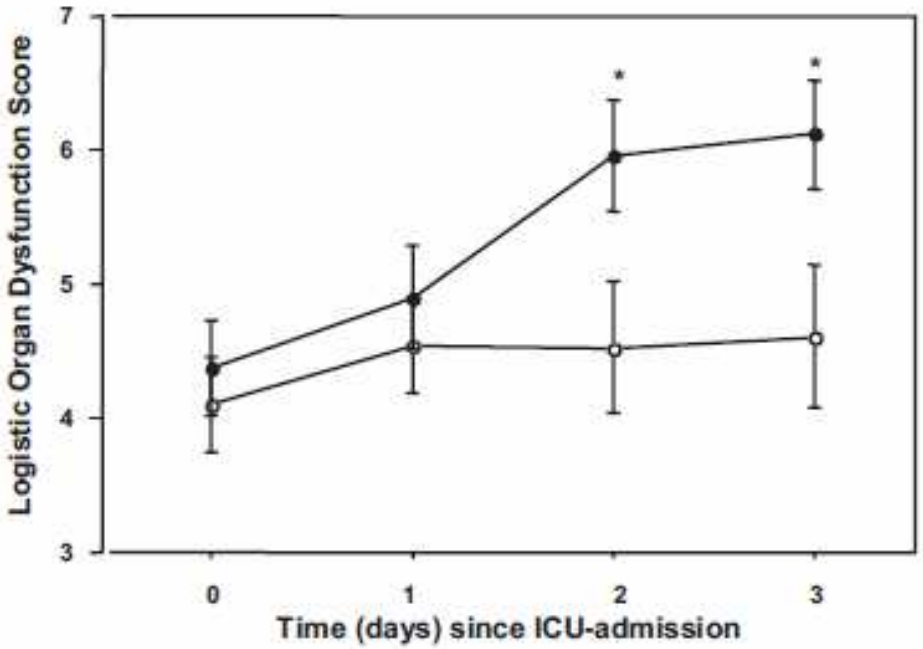

Figure 2. Changes in Organ Logistic Dysfunction Scores (means ± SD) throughout the first 3 intensive care unit (*ICU*) days. *Black circle*: noninvasive ventilation failure. *Open circle*: noninvasive ventilation success. *$p < 0.03$.

A multiple-center survey on the use in clinical practice of noninvasive ventilation as a first-line intervention for acute respiratory distress syndrome*

Table 5. Univariate and multivariate analysis of risk factors for endotracheal intubation

Variable	No. of Endotracheal Intubations/Total (%)	Univariate Analysis			Multivariate Analysis		
		OR	95% CI	*p* Value[a]	OR	95% CI	*p* Value[a]
Age, yrs							
≤58	28/77 (36)	1			1		
>58	40/70 (57)	2.33	1.2–4.52	.01	1.4	0.66–3	.38
Gender, male	50/93 (54)	2.38	1.18–4.78	.01	2.1	0.93–4.64	.07
SAPS II							
≤34	25/78 (32)	1			1		
>34	43/69 (62)	3.5	1.77–6.92	.0003	3.6	1.66–7.7	.001
Δ RR							
>4	32/89 (36)	1			1		
4	36/58 (62)	2.91	1.47–5.78	.002	1.94	0.86–4.36	.1
pH after 1 hr							
>7.37	25/75 (33)	1			1		
≤7.37	43/72 (60)	2.96	1.51–5.8	.001	1.91	0.85–4.31	.11
Pao_2/Fio_2 after 1 hr							
>175	28/79 (35)	1			1		
≤175	40/68 (59)	2.92	1.49–5.72	.001	2.34	1.1–5.15	.03

Massimo Antonelli, MD **(Crit Care Med 2007; 35:18–25)**

Non-invasive ventilation…

Start « early » …

… for a potentially rapidly reversible complication…

… for a couple of hours !

= 10-15 % of the population..!

Support Care Cancer (2006) 14: 167–171
DOI 10.1007/s00520-005-0845-0

ORIGINAL ARTICLE

Anne-Pascale Meert
Thierry Berghmans
Michel Hardy
Eveline Markiewicz
Jean-Paul Sculier

Non-invasive ventilation for cancer patients with life-support techniques limitation

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Abstract *Goals of work:* The study was conducted to determine the usefulness and efficacy of non-invasive ventilation (NIV) in cancer patients with "life-support techniques limitation" admitted for an acute respiratory distress, in terms of intensive care unit (ICU) and hospital discharges. *Patients and methods:* A total of 18 consecutive cancer patients (17 with solid tumours and one with haematological malignancy) with "life-support techniques limitation" in acute respiratory failure and who benefited from NIV were included. NIV was provided with a standard face mask by the BiPAP Vision ventilator (Respironics Inc.). Variables related to the demographic parameters, SAPS II score, cancer characteristics, intensive care data and hospital discharge were recorded. *Main results:* Complications leading to NIV were hypoxemic respiratory failure in 11 patients and hypercapnic respiratory failure in seven. Total median duration of NIV was 29 h. NIV was applied during a median of 2.5 days with a median of 16 h per day. Total median ICU stay was 7 days (range 1–21). Fourteen and ten patients were discharged from ICU and from hospital, respectively. *Conclusion:* NIV appears to be an effective ventilation support for cancer patients with "life-support techniques limitation".

Keywords Neoplasm · Non-invasive ventilation · Respiratory failure · Life support techniques limitation · Cancer

Conclusion

Intensive Care Med (2010) 36:1633–1635
DOI 10.1007/s00134-010-1949-7

EDITORIAL

Dominique D. Benoit
Pieter O. Depuydt

Non-invasive ventilation in patients with hematological malignancies: the saga continues, but where is the finale?

La ventilation non-invasive (VNI) réduit le risque d'intubation et la mortalité chez le cancereux avec une IRA

Oui

Non

La ventilation non-invasive (VNI) devrait être utiliser d'emblé chez le sujet cancereux avec une IRA ne présentant pas de contre-indications classiques

Oui

Non

Medicine is learned by the bedside and not in the classroom. Let not your conceptions of disease come from words heard in the lecture room or read from the book. See, and then reason, and compare and control. But see first

Sir William Osler – 1904