Syndrome de Détresse Respiratoire Aiguë

Sédation & Curarisation

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The Lancet · Saturday 12 August 1967

ACUTE RESPIRATORY DISTRESS IN ADULTS

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ANESTHESIA AND ANALGESIA . . . *Current Researches* VOL. 54, NO. 2, MARCH-APRIL, 1975

The Adult Respiratory Distress Syndrome and Pancuronium Bromide

RICHARD W. LIGHT, M.D.*
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RONALD B. GEORGE, M.D.

Diagnosis and Clinical Course of 6 Patients Given Pancuronium Bromide During Artificial Ventilation

Case	Diagnosis	Pancuronium dose		Duration of paralysis, hr.	Side effects	Outcome
		Initial, mg.	Maintenance, mg./2 hr.			
1	Heroin overdose	5	2	90	Amnesia	Full recovery
2	Heroin overdose	5	2	30	Muscle soreness, terrified	Full recovery
3	Heroin overdose	10	1	20	Muscle soreness	Full recovery
4	Fat emboli	5	1.5	120	—	Died without regaining consciousness
5	Heroin overdose	5	1.5	36	None	Full recovery
6	Heroin and secobarbital overdose	5	1	18	Amnesia	Full recovery

Anesthesiology
60:369–371, 1984

Hemodynamic and Gas Exchange Effects of Pancuronium Bromide in Sedated Patients with Respiratory Failure

MICHAEL J. BISHOP, M.D.*

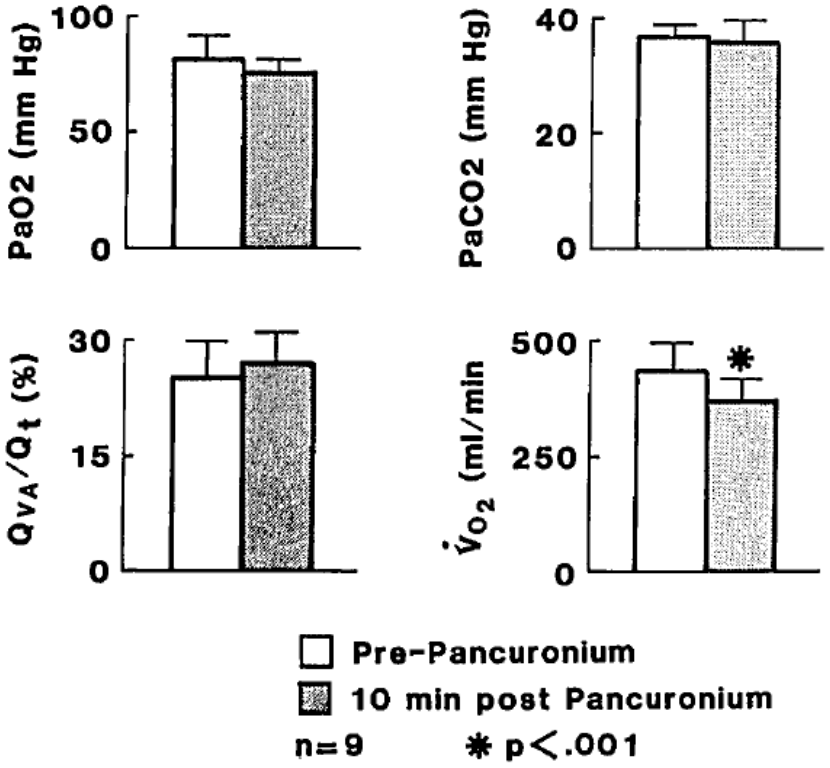

FIG. 1. Gas exchange before and 10 minutes after pancuronium as measured by Pa_{O_2}, Pa_{CO_2}, venous admixture ($\dot{Q}_{VA}/\dot{Q}_t$), and oxygen consumption ($\dot{V}_{O_2}$). All values are means ± SEM.

TABLE 2. Hemodynamic Changes after Pancuronium

Control	Before Pancuronium	After Pancuronium	*P*
Heart rate (beats/m)	118 ± 5	132 ± 17	0.006
Cardiac output (l/m)	6.56 ± 0.67	6.60 ± 0.90	>0.1
Blood pressure (mmHg)	76 ± 8	90 ± 9	0.06
Pulmonary artery pressure (mmHg)	28 ± 4	31 ± 4	0.01
Pulmonary artery wedge pressure (mmHg)	16 ± 2	16 ± 2	>0.1
Stroke volume (ml/beat)	56 ± 6	50 ± 7	0.004
Systemic resistance ($dyne \cdot s \cdot cm^{-5}$)	987 ± 106	1221 ± 164	0.04
Pulmonary vascular resistance ($dyne \cdot s \cdot cm^{-5}$)	163 ± 33	205 ± 38	0.004

Values are means ± SEM.

ARDS: Objectifs de la sédation

- Confort :
  - Analgésie et anxiolyse
  - Adaptation suffisante au ventilateur

- Thérapeutique :
  - Permettre des réglages « non physiologiques », éviter le risque d'asynchronisme
  - ⬇ Consommation d'O2

- Niveau:
  - Optimale = minimale efficace pour éviter les curares et les VILI
  - Rendre possible la curarisation si nécessaire

Niveau de sédation

- Haut niveau de sédation souvent nécessaire pour traiter la détresse respiratoire et la désynchronisation patient-ventilateur
- Ventilation protectrice : priorité

- Sédation optimale du SDRA = sédation profonde ?

Kallet R et al Respir Care. 2001;46:1024-37

Quand et pourquoi une sédation lors du SDRA

- Recommandations SFAR-SRLF 2005, Sédation, analgésie et curarisation :
  - Modalités d'usage et choix des agents hypnotiques et analgésiques.

- Contraintes ventilatoires lors du SDRA:
  - +++ En raison de l'hypoxémie majeure

- Objectifs de la sédation:
  - Assurer un confort suffisant du patient sans risque de désadaptation patient-ventilateur » (accord fort des experts).

Quand et pourquoi une sédation lors du SDRA

- Adaptation du patient au ventilateur
  - Réduit risque barotraumatisme ou dérecrutement.
  - Posologie minimale efficace (optimale)
    - ✓ Doit être recherchée dés l'instauration de la sédation
    - ✓ Adaptée très régulièrement, au besoin plusieurs fois par jour (accord fort des experts).

- Réduction des besoins ventilatoires
  - Diminution production de CO2 (accord fort des experts).

Quand et pourquoi une sédation lors du SDRA

- Réduction de la consommation globale en O2
  - Directement liée à une mise au repos du système respiratoire lors de la sédation
  - Amélioration significative état hémodynamique de patients dont la consommation en O2 des muscles respiratoires était très élevée .

- Au total, les experts suggèrent que
  - Sédation optimale = sédation profonde
  - Adaptation parfaite du patient au ventilateur
  - Mise au repos des muscles respiratoires.
  - Mais attitude empirique non confirmée par aucune étude

Effect of neuromuscular blocking agents on gas exchange in patients presenting with acute respiratory distress syndrome*

Marc Gainnier, MD; Antoine Roch, MD; Jean-Marie Forel, MD; Xavier Thirion, MD, Ph
Jean-Michel Arnal, MD; Stéphane Donati, MD; Laurent Papazian, MD, PhD

Crit Care Med 2004 Vol. 32, No. 1

- 56 patients, SDRA randomisés en deux groupes :
  - Gr. témoin: prise en charge ventilatoire classique sans curarisation
  - Gr. curarisé par cisatracurium
  - Même prise en charge pendant les 48 premières heures.
- Tous les patients: sédation par midazolam – Sufenta QSP une sédation profonde (score de Ramsay 6).

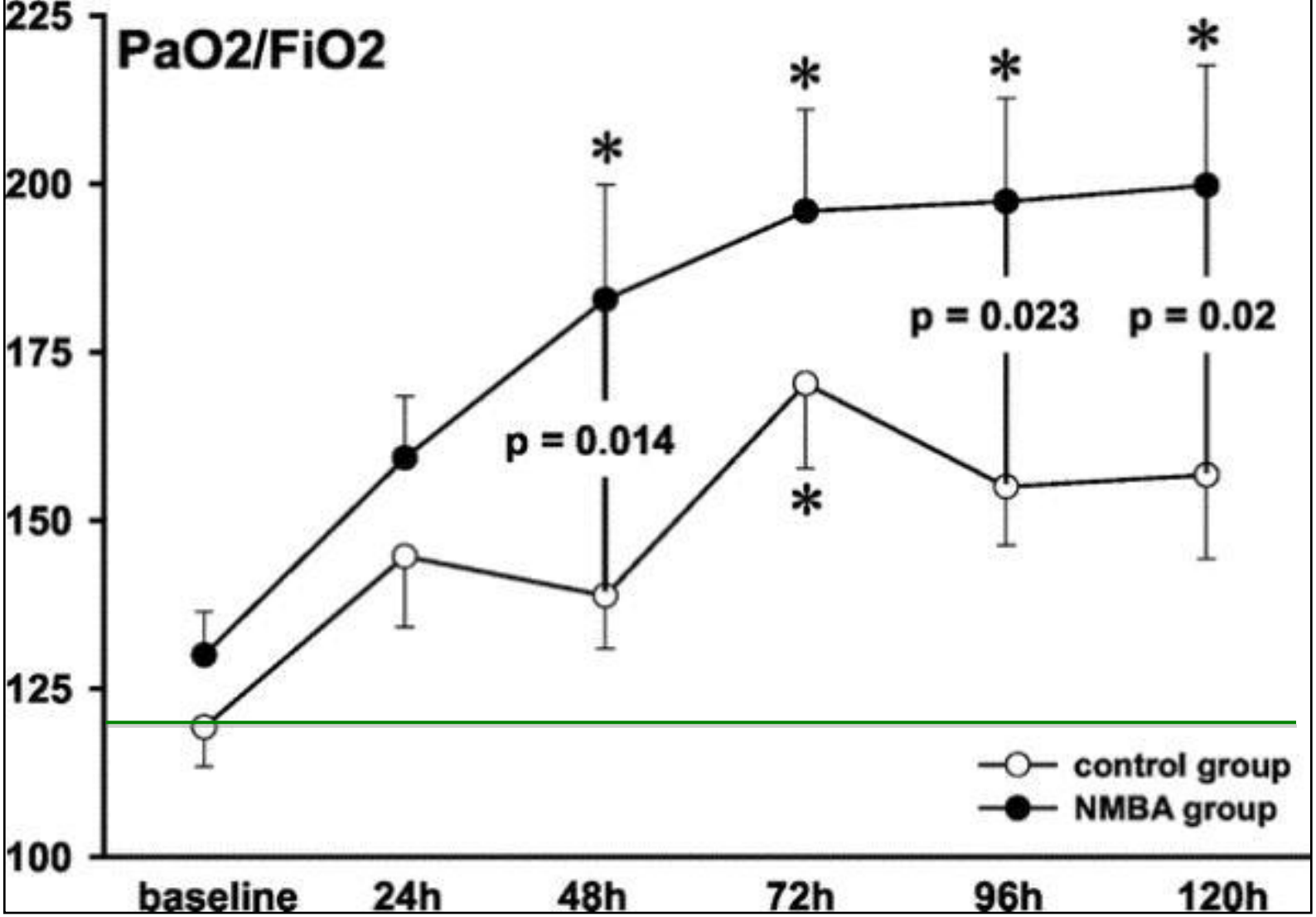

Figure 1. Evolution of Pao2/Fio2 during the 120-hr period of the study.

Results are expressed as mean +/- sem. NMBA, neuromuscular blocking agents; *p < .001 vs. baseline by Tukey test.

Effect of neuromuscular blocking agents on gas exchange in patients presenting with acute respiratory distress syndrome*

Marc Gainnier, MD; Antoine Roch, MD; Jean-Marie Forel, MD; Xavier Thirion, MD, Ph
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Crit Care Med 2004 Vol. 32, No. 1

- 56 patients, SDRA randomisés en deux groupes :
  - Gr. témoin: prise en charge ventilatoire classique sans curarisation
  - Gr. curarisé par cisatracurium et bénéficiant de la même prise en charge pendant les 48 premières heures.
- Tous les patients: sédation par midazolam – Sufenta QSP une sédation profonde (score de Ramsay 6).

- Même en l'absence de curarisation
  - Amélioration progressive oxygénation patients bénéficiant d'une prise en charge ventilatoire optimisée avec sédation profonde.

- En contradiction avec études suggérant que le pronostic vital peut être aggravé en approfondissant le niveau de sédation (augmentation dose agents sédatifs).

The Use of Continuous IV Sedation Is Associated With Prolongation of Mechanical Ventilation*

CHEST 1998; 114:541–548

Marin H. Kollef, MD, FCCP; Nat T. Levy, MD; Thomas S. Ahrens, DNSc; Robyn Schaiff, PharmD; Donna Prentice, MSN; and Glenda Sherman, RN

- Etude prospective observationnelle, sédation IV continue et éventuelle majoration de la durée de ventilation mécanique.

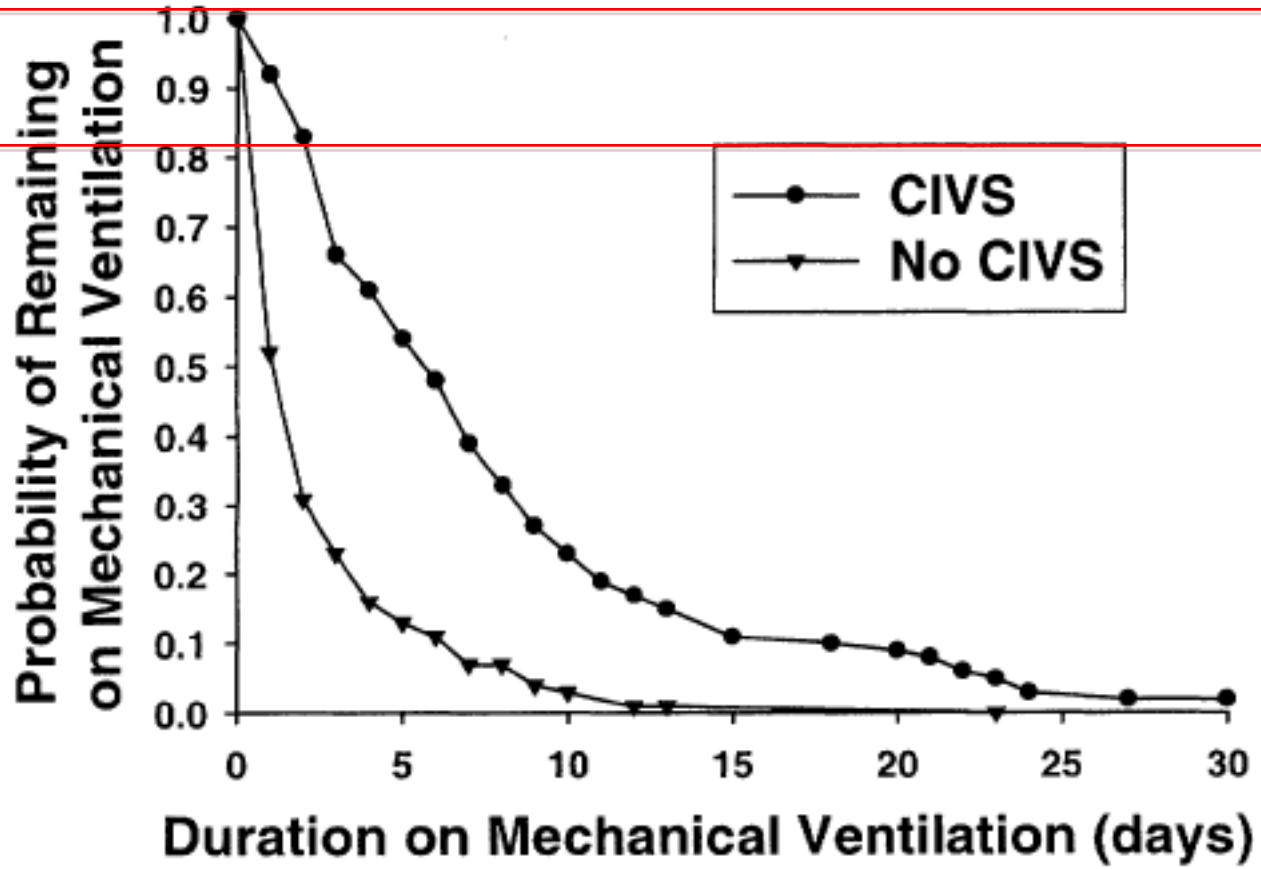
- 242 patients consécutifs ventilés, 93 pts sédation continue IVSE, 149 sédation par boli.

- Critère de jugement principal: durée de ventilation mécanique.

Variable	Continuous IV Sedation (n=93)	No Continuous IV Sedation (n=149)	p Value
Baseline characteristics			
Age, yr	48.8±16.8	60.9±16.3	<0.001
Gender, No. (%)			
Male	42 (45.2)	79 (53.0)	0.234
Female	51 (54.8)	70 (47.0)	
Race, No. (%)			
White	57 (61.3)	71 (47.7)	0.071
Black	34 (36.6)	76 (51.0)	
Other	2 (2.1)	2 (1.3)	
COPD, No. (%)	40 (43.0)	47 (31.5)	0.071
Congestive heart failure, No. (%)	5 (5.4)	7 (4.7)	0.813
Underlying malignancy, No. (%)	18 (19.4)	29 (19.5)	0.983
APACHE II score	20.2±6.5	21.2±8.9	0.702
Predicted mortality	35.8±22.1	38.9±28.3	0.702
PaO_2/FIO_2	175±107	232±152	0.005
Indication for Mechanical Ventilation			
Pneumonia, No. (%)	22 (23.7)	27 (18.1)	0.297
Drug overdose, No. (%)	5 (5.4)	15 (10.1)	0.197
ARDS or ALI, No. (%)	18 (19.4)	15 (10.1)	0.041
COPD/asthma, No. (%)	22 (23.7)	33 (22.2)	0.785
Pulmonary edema, No. (%)	11 (11.8)	16 (10.7)	0.793
Cardiac arrest, No. (%)	5 (5.4)	16 (10.7)	0.149
Pulmonary embolus, No. (%)	4 (4.3)	6 (4.0)	>0.999
Other, No. (%)	6 (6.4)	21 (14.1)	0.066

Variable	Continuous IV Sedation (n=93)	No Continuous IV Sedation (n=149)	p Value
Continuous infusion agent, No. (%)			
Lorazepam	25 (26.9)	—	
Fentanyl	24 (25.8)	—	
Propofol	2 (2.1)	—	
Lorazepam+fentanyl	42 (45.2)	—	
Duration of continuous infusion, d	6.0±6.4	—	
Bolus sedation, No. (%)	66 (71.0)	64 (42.9)	<0.001
Bolus infusion agent, No. (%)			
Lorazepam	16 (17.2)	14 (9.4)	0.073
Fentanyl	9 (9.7)	7 (4.7)	0.129
Midazolam	5 (5.4)	8 (5.4)	0.998
Morphine	3 (3.2)	1 (0.7)	0.160
Lorazepam+fentanyl	32 (34.4)	33 (22.2)	0.036
Haloperidol	1 (1.1)	1 (0.7)	>0.999
Duration of bolus sedation, d	2.3±3.6	1.6±0.7	0.389
Bolus doses administered	4.6±5.4	3.7±2.5	0.901
Chemical paralysis, No. (%)	12 (12.9)	0 (0.0)	<0.001
Duration of chemical paralysis, d	4.0±3.4	—	

Outcor	p Value
Duration of mechani	<0.001
Length of intensive c	<0.001
Length of hospital st	<0.001
Acquired organ syste	0.018
Reintubation, No. (%	0.005
Tracheostomy, No. (	0.080
Hospital mortality, N	0.576



La sédation en perfusion continue est un facteur de risque indépendant associé avec une prolongation de la durée de la ventilation mécanique.

CHEST 1998; 114:541–548

DAILY INTERRUPTION OF SEDATIVE INFUSIONS IN CRITICALLY ILL PATIENTS UNDERGOING MECHANICAL VENTILATION

JOHN P. KRESS, M.D., ANNE S. POHLMAN, R.N., MICHAEL F. O'CONNOR, M.D., AND JESSE B. HALL, M.D.

N Engl J Med 2000;342:1471-1477.

ASSIGNED SEDATIVE DRUG	PROTOCOL
Midazolam	Midazolam: initial intravenous bolus of 0.5–5 mg every 1–5 min as needed
	Midazolam: continuous infusion at 1–2 mg/hr; dosage to be increased in increments of 1–2 mg/hr until adequate sedation is achieved
	Morphine: initial intravenous bolus of 2–10 mg as needed
	Morphine: continuous infusion at 1–5 mg/hr
Propofol	Propofol: continuous infusion at 5 μg/kg of body weight/min; dosage to be increased in increments of 5–10 μg/kg/min every 2 min until adequate sedation is achieved
	Morphine: initial intravenous bolus of 2–10 mg as needed
	Morphine: continuous infusion at 1–5 mg/hr

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N Engl J Med 2000;342:1471-1477.

VARIABLE	INTERVENTION GROUP (N=68)	CONTROL GROUP (N=60)	P VALUE
Age (yr)			0.57
Median	57	61	
Interquartile range	42–71	40–74	
Sex (no.)			0.56
Male	34	26	
Female	34	34	
Weight (kg)			0.70
Median	69.9	66.0	
Interquartile range	58.9–90.2	60.4–78.8	
APACHE II score*			0.30
Median	20	22	
Interquartile range	15–25	16–25	
Permissive hypercapnia (no.)	12	15	0.42
Diagnosis (no.)			
Acute respiratory distress syndrome or pulmonary edema	20	15	0.72
Chronic obstructive pulmonary disease or ventilatory failure	22	17	0.76
Asthma	4	3	0.86
Sepsis	10	15	0.21
Delirium	8	5	0.73
Hemorrhagic shock	1	3	0.52
Cardiogenic shock	2	2	0.70
Drug overdose	1	0	0.95

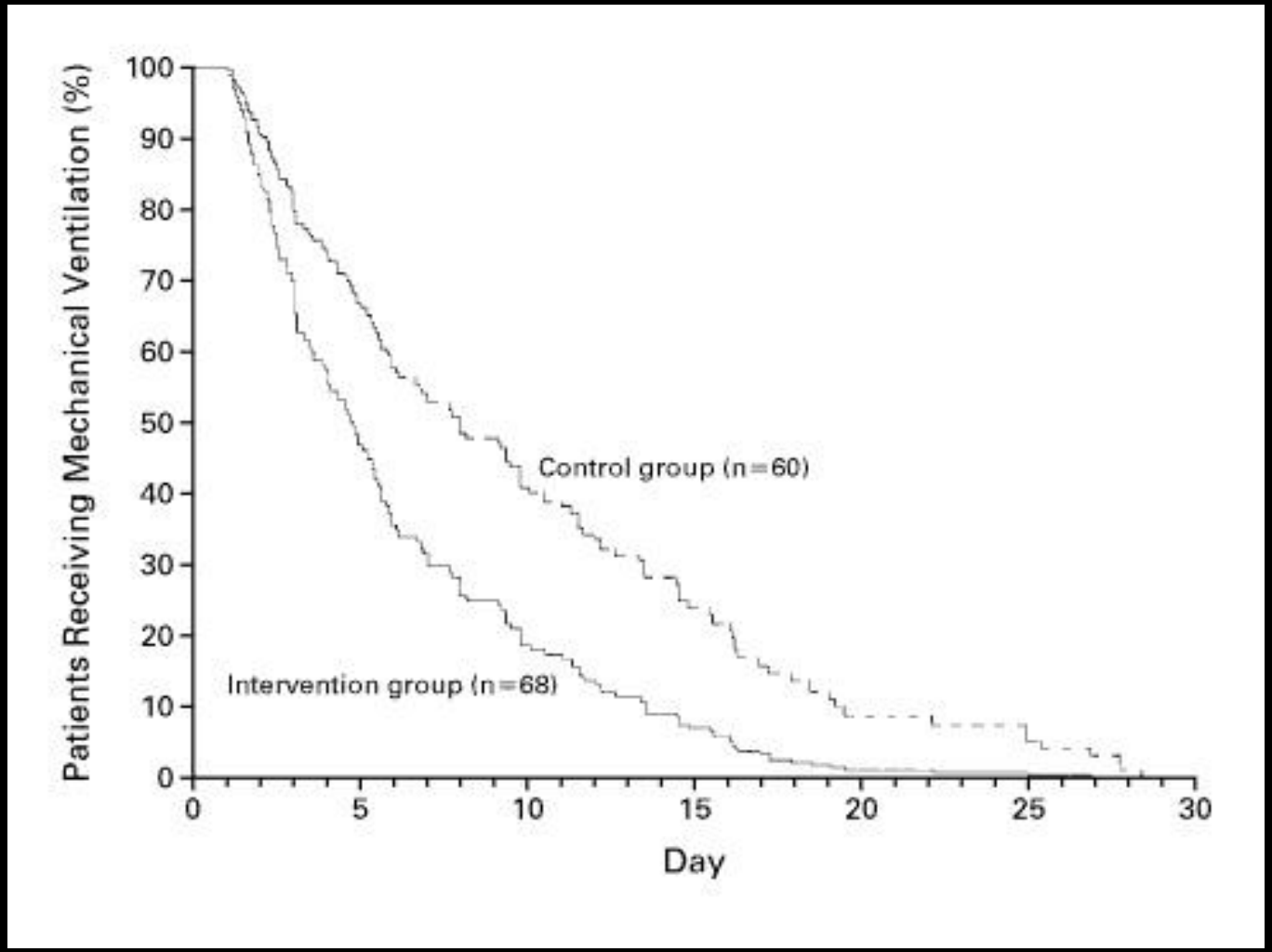
DAILY INTERRUPTION OF SEDATIVE INFUSIONS IN CRITICALLY ILL PATIENTS UNDERGOING MECHANICAL VENTILATION

JOHN P. KRESS, M.D., ANNE S. POHLMAN, R.N., MICHAEL F. O'CONNOR, M.D., AND JESSE B. HALL, M.D.

N Engl J Med 2000;342:1471-1477.

VARIABLE	INTERVENTION GROUP (N=68)	CONTROL GROUP (N=60)	P VALUE
	median (interquartile range)		
Duration of mechanical ventilation (days)	4.9 (2.5–8.6)	7.3 (3.4–16.1)	0.004
Length of stay (days)			
Intensive care unit	6.4 (3.9–12.0)	9.9 (4.7–17.9)	0.02
Hospital	13.3 (7.3–20.0)	16.9 (8.5–26.6)	0.19
Midazolam subgroup (no. of patients)	37	29	
Total dose of midazolam (mg)	229.8 (59–491)	425.5 (208–824)	0.05
Average rate of midazolam infusion (mg/kg/hr)	0.032 (0.02–0.05)	0.054 (0.03–0.07)	0.06
Total dose of morphine (mg)	205 (68–393)	481 (239–748)	0.009
Average rate of morphine infusion (mg/kg/hr)	0.027 (0.02–0.04)	0.05 (0.04–0.07)	0.004
Propofol subgroup (no. of patients)	31	31	
Total dose of propofol (mg)	15,150 (3983–34,125)	17,588 (4769–35,619)	0.54
Average rate of propofol infusion (mg/kg/hr)	1.9 (0.9–2.6)	1.4 (0.9–2.4)	0.41
Total dose of morphine (mg)	352 (108–632)	382 (148–1053)	0.33
Average rate of morphine infusion (mg/kg/hr)	0.035 (0.02–0.07)	0.043 (0.02–0.07)	0.65

Kaplan–Meier Analysis of the Duration of Mechanical Ventilation, According to Study Group.



Kress JP et al. N Engl J Med 2000;342:1471-1477.

Effets physiopathologiques supposés des curares dans le SDRA

- Blocage neuromusculaire
  - Augmentation de la compliance thoraco-pulmonaire
  - Meilleure adaptation au ventilateur
  - Inhibition activité musculaire expiratoire.

- Augmentation capacité résiduelle fonctionnelle
- Diminution du shunt intra-pulmonaire.

- Changements rapports ventilation/perfusion
  - Distribution plus homogène perfusion pulmonaire
  - Application de plus faibles pressions pulmonaires
  - Favorisent perfusion zones ventilées et diminuent shunt intra-pulm.

Tokics, J. Appl. Physiol. 1996

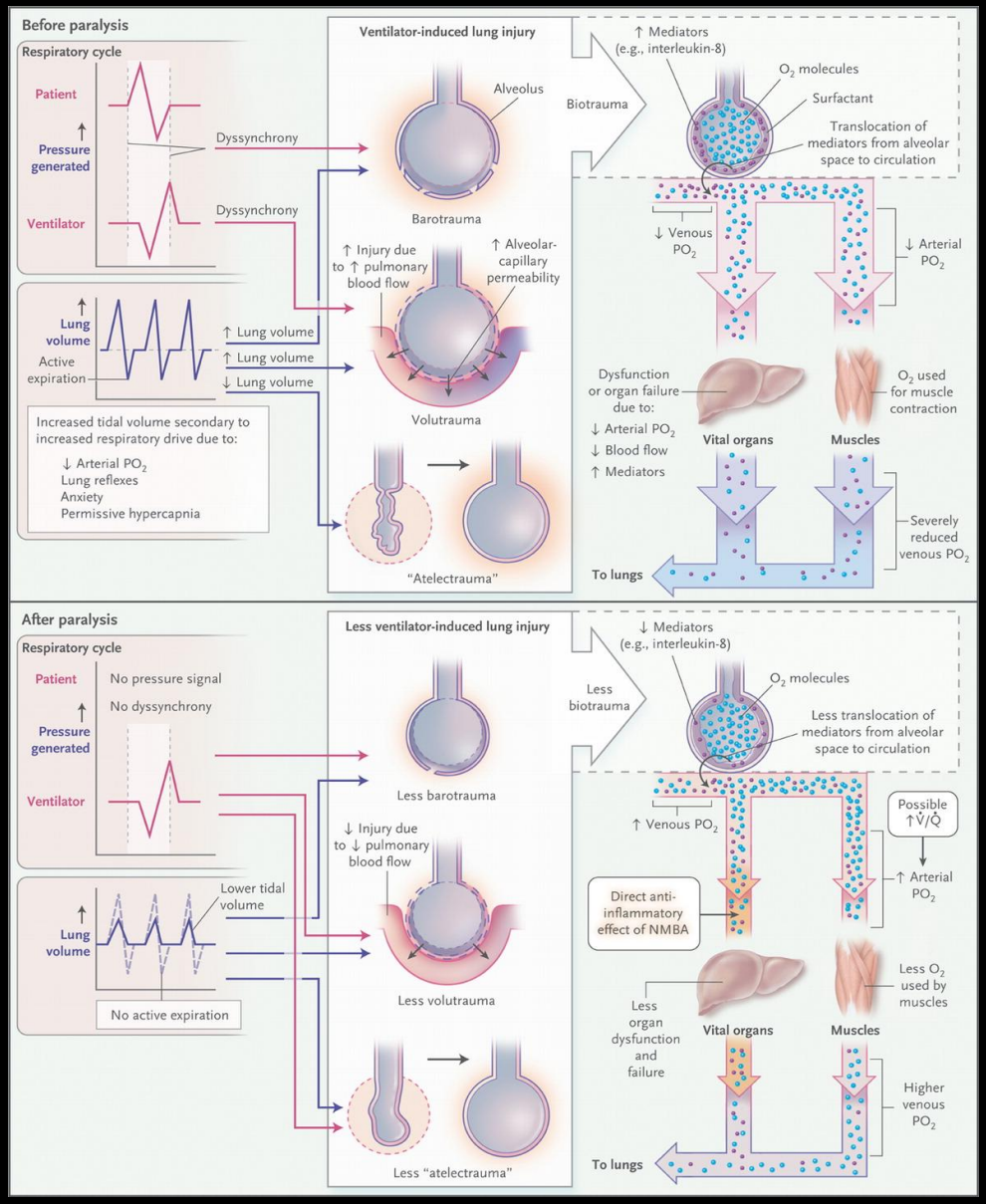
Effets physiopathologiques supposés des curares dans le SDRA

- Meilleure distribution régionale Vt
  - ↓ surdistension territoires à compliance conservée
  - +++ recrutement territoires à faible compliance.

- Absence d'asynchronie patient/ventilateur
  - Limite pressions trans-pulmonaires pendant les efforts inspiratoires
  - Diminue collapsus expiratoire:
    - Inhibe expiration active
    - Limite dérecrutement
    - Permet maintien PEEP

Slutsky. *N. Engl. J. Med.*, 2010

Possible Mechanisms by Which Neuromuscular Blocking Agents (NMBAs) Might Lead to Improved Survival in Patients with the Acute Respiratory Distress Syndrome (ARDS).



Slutsky AS. N Engl J Med 2010;363:1176-1180.

The NEW ENGLAND JOURNAL of MEDICINE

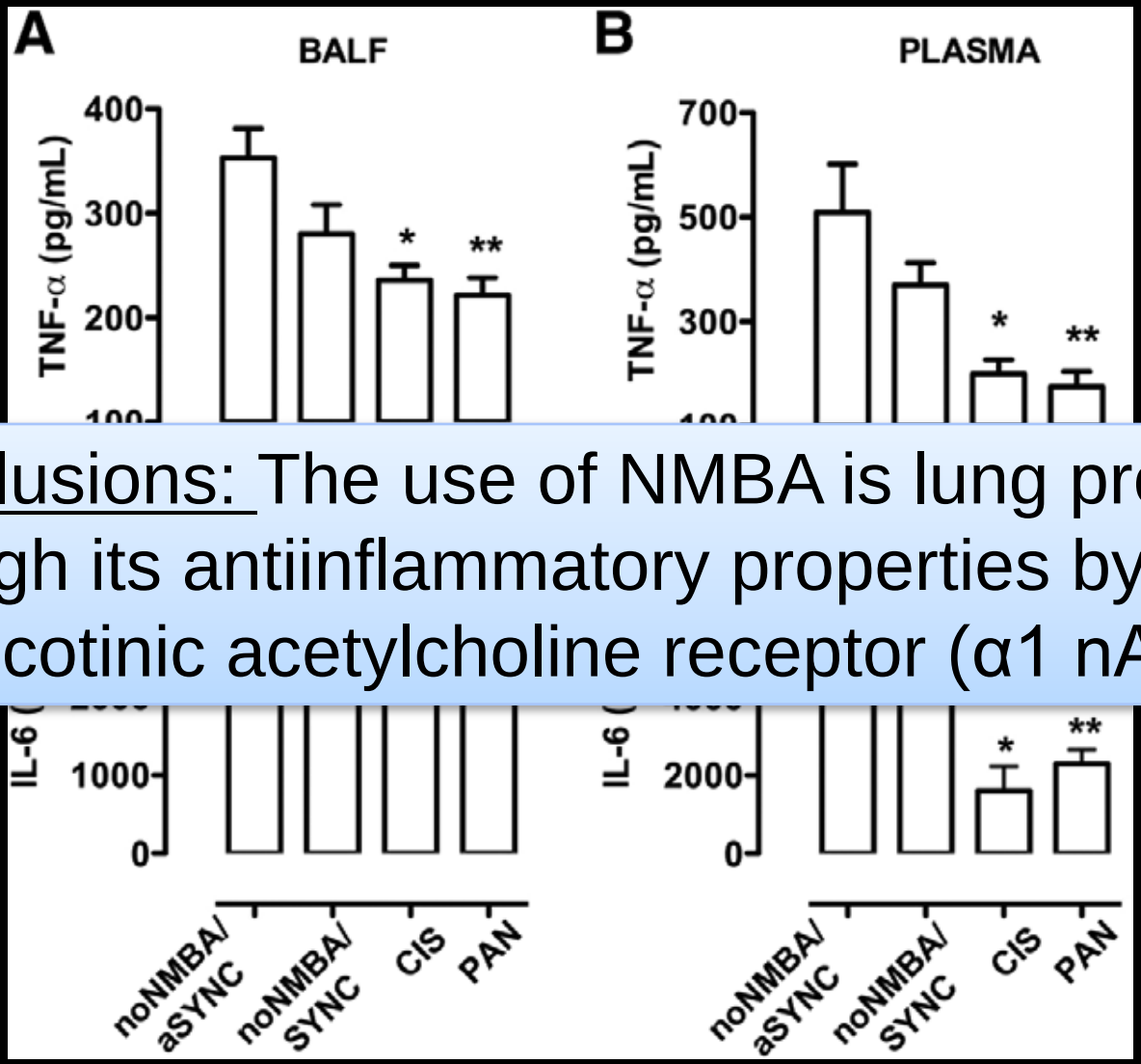
Neuromuscular Blocking Agent Cisatracurium Attenuates Lung Injury by Inhibition of Nicotinic Acetylcholine Receptor-α1 (ANESTHESIOLOGY 2016; 124:00-00)

Vito Fanelli, M.D., Ph.D., Yasumasa Morita, M.D., Ph.D., Paola Cappello, Ph.D., Mirna Ghazarian, M.Sc., Bina Sugumar, B.Sc., Luisa Delsedime, M.D., Jane Batt, M.D., Ph.D., V. Marco Ranieri, M.D., Haibo Zhang, M.D., Ph.D., Arthur S. Slutsky, M.D.

Evaluate the inflammatory responses that may be modulated by NMBA using a rat and mouse model of lung injury

Nicotinic acetylcholine receptors, mediate proinflammatory effects in a variety of cell types

Nicotinic acetylcholine receptors are antagonized by NMBA



Conclusions: The use of NMBA is lung protective through its antiinflammatory properties by blocking the nicotinic acetylcholine receptor (α1 nAChRα1).

(Anesthesiology 2016; 124:00-00)

Effets physiopathologiques supposés des curares dans le SDRA

- Rôle protecteur contre les lésions induites par VM (VILI):
  - ✓ Diminution incidence des barotraumatismes
  - ✓ Baisse production de cytokines pro-inflammatoires dans le poumon et dans le sang

Neuromuscular blocking agents decrease inflammatory response in patients presenting with acute respiratory distress syndrome*

Jean-Marie Forel, MD; Antoine Roch, MD, PhD; Valérie Marin, MD, PhD; Pierre Michelet, MD; Didier Demory, MD; Jean-Louis Blache, MD; Gilles Perrin, MD; Marc Gainnier, MD. PhD: Pierre Bongrand, MD, PhD; Laurent Papazian, MD, PhD

Crit Care Med 2006 Vol. 34, No. 11

- Evaluation inflammation pulmonaire et systémique
- 36 patients en SDRA, ventilation protectrice
- Perfusion continue de cisatracurium ou un placebo à la phase précoce.
- Dosage marqueurs inflammation dans le LBA et le sérum.

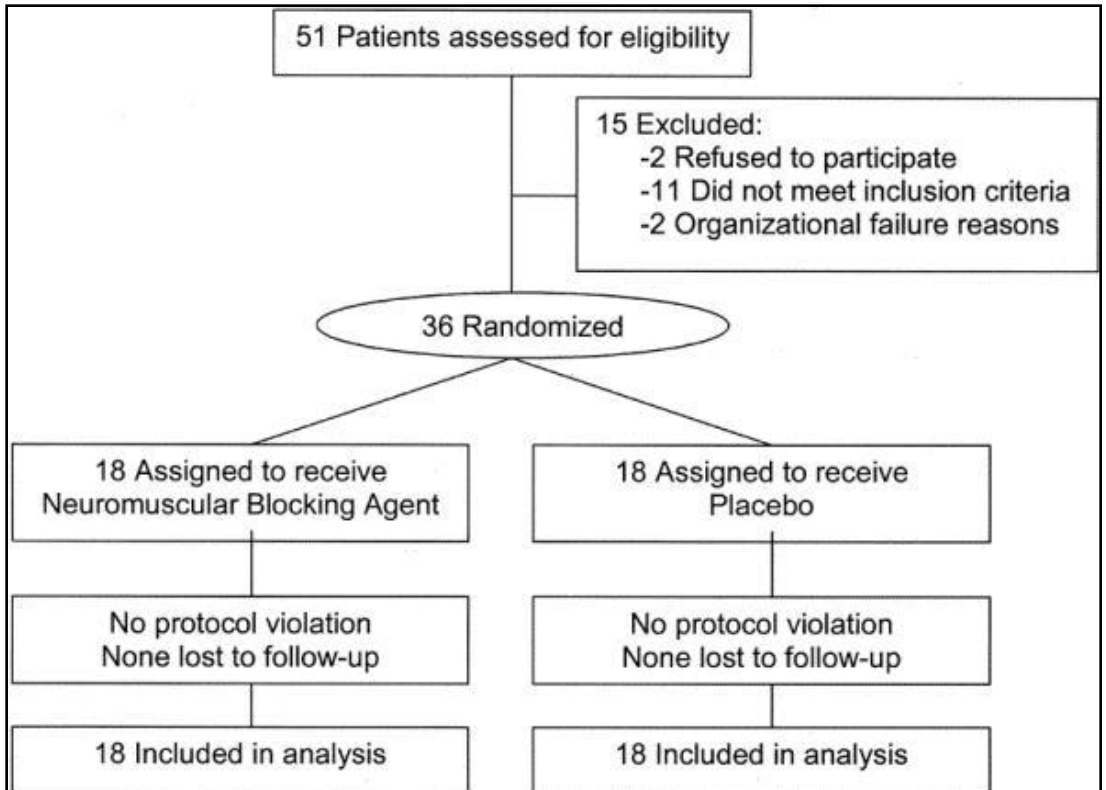


Table 1. Characteristics of the patients at inclusion

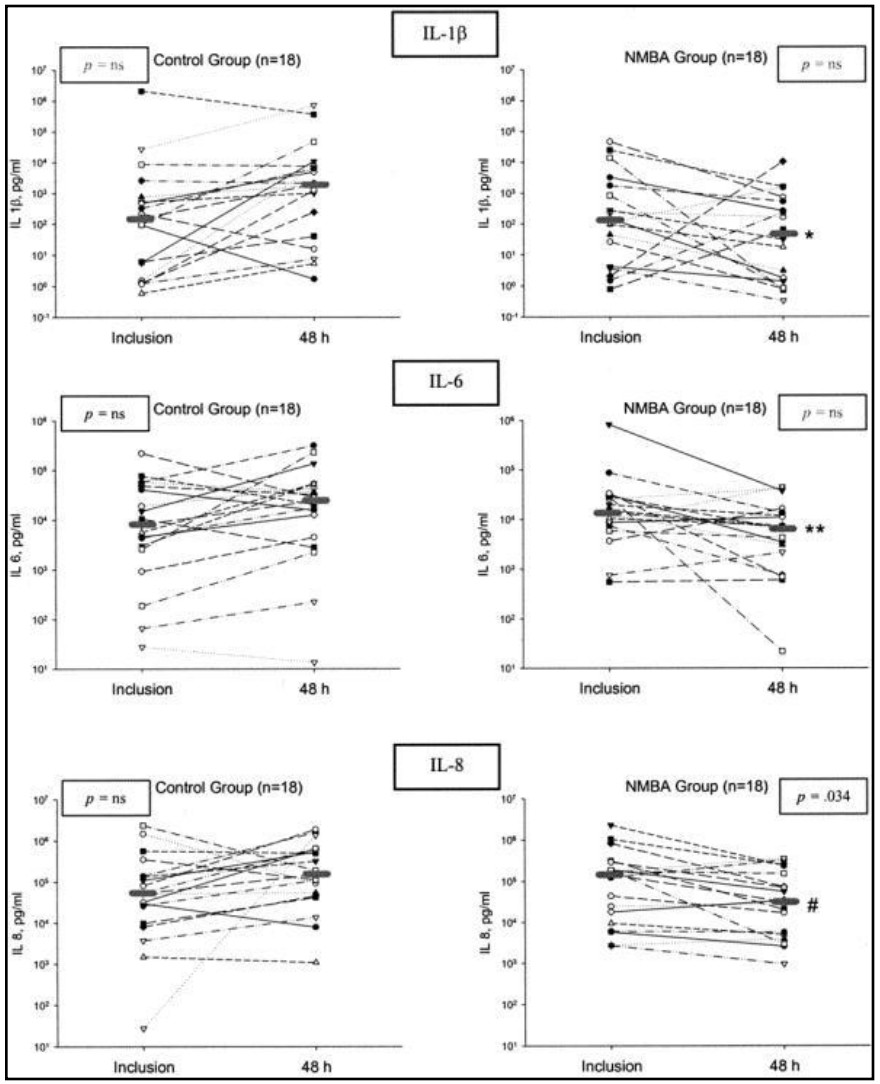
	Control Group (n = 18)	NMBA Group (n = 18)	p
Age, yrs	61 ± 18	52 ± 16	NS
Men, n (%)	12 (67)	14 (78)	NS
SAPS II	49 ± 19	47 ± 15	NS
Cause of ARDS, n (%)			
Pneumonia	13 (72)	15 (83)	NS
Lung contusion	1 (6)	0 (0)	NS
Extrapulmonary sepsis	4 (22)	3 (17)	NS
ARDS with direct lung injury, n (%)	14 (78)	15 (83)	NS
Lung injury severity score	2.8 ± 0.4	3.0 ± 0.2	NS
Duration of ARDS before randomization, days	1.2 ± 0.8	1.0 ± 0.8	NS
Septic shock associated with ARDS, n (%)	13 (72)	13 (72)	NS

NMBA, neuromuscular blocking agents; NS, not significant; SAPS, Simplified Acute Physiology Score, higher values indicate greater severity; ARDS, acute respiratory distress syndrome.

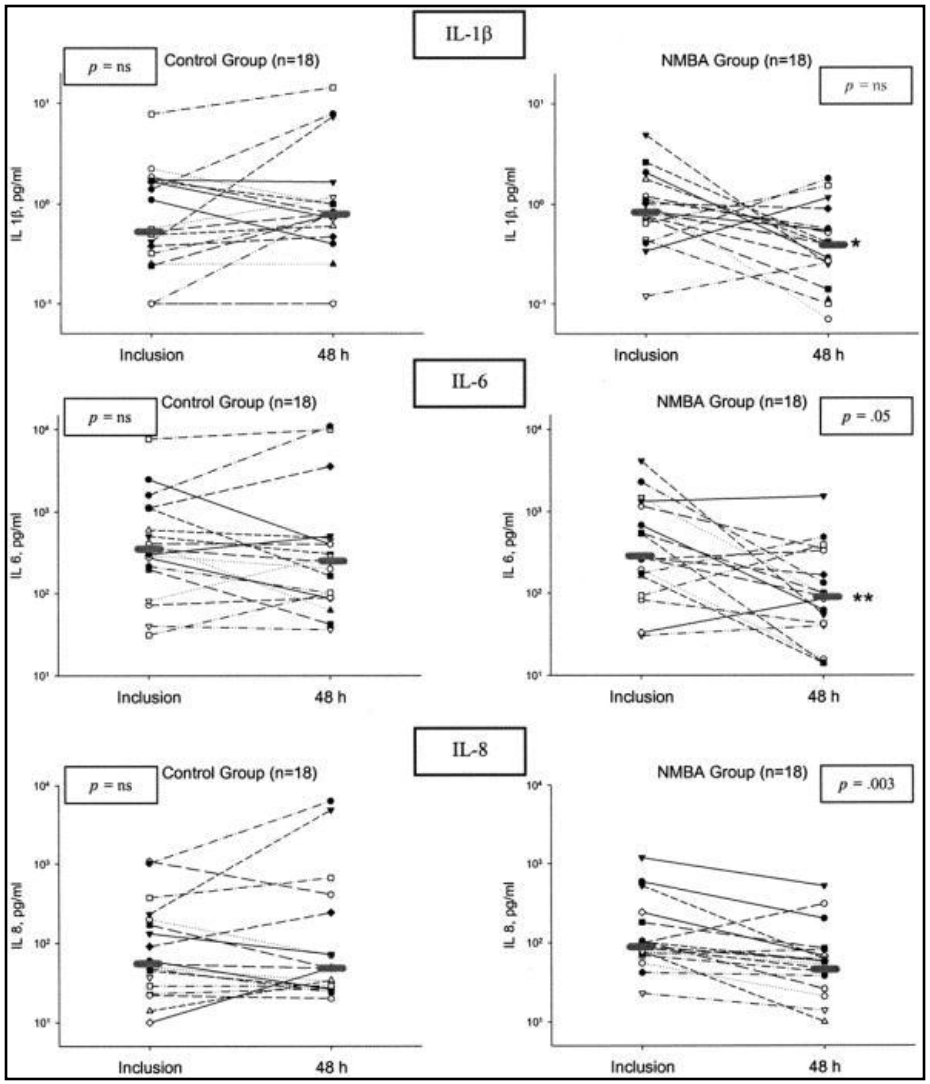
Values are expressed as mean ± SD or number of cases (percentage); inclusion was the time just before drug administration; lung injury severity score, higher values indicate greater severity; septic shock was defined as a systolic blood pressure of <90 mm Hg, despite adequate volume expansion requiring the use of vasopressor agents and associated with a proven or suspected infection.

Forel. Crit Care Med 2006

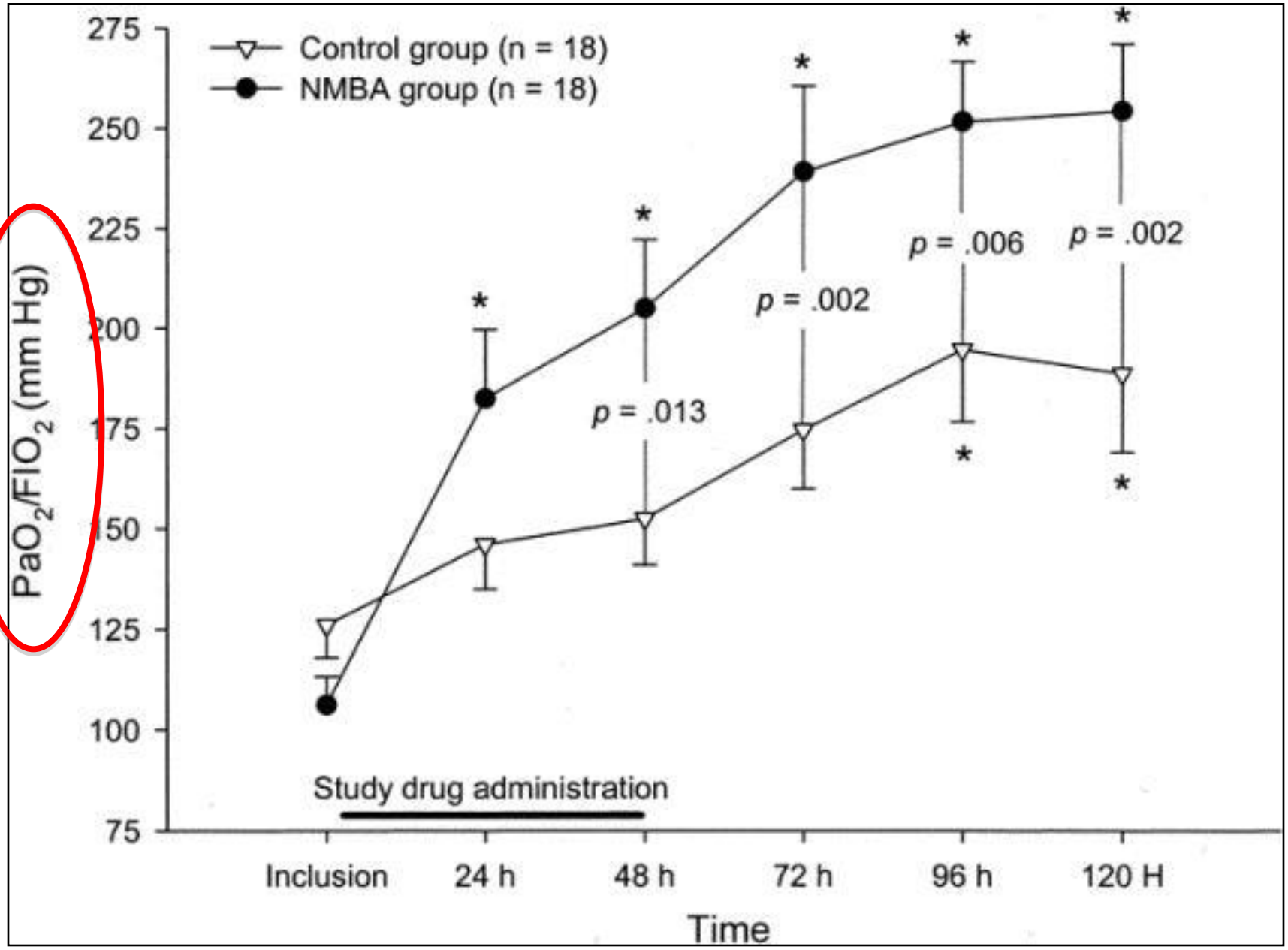
LBA



Plasma



Forel. Crit Care Med 2006



Forel. Crit Care Med 2006

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Crit Care Med 2004 Vol. 32, No. 1

- 56 patients, SDRA randomisés en deux groupes :
  - Gr. témoin: prise en charge ventilatoire classique sans curarisation
  - Gr. curarisé par cisatracurium pendant 48h
  - Même prise en charge pendant les 48 premières heures.
  - Vt de 6-8 ml / kg de poids corporel idéal.

Table 1. Characteristics of Patients at Inclusion

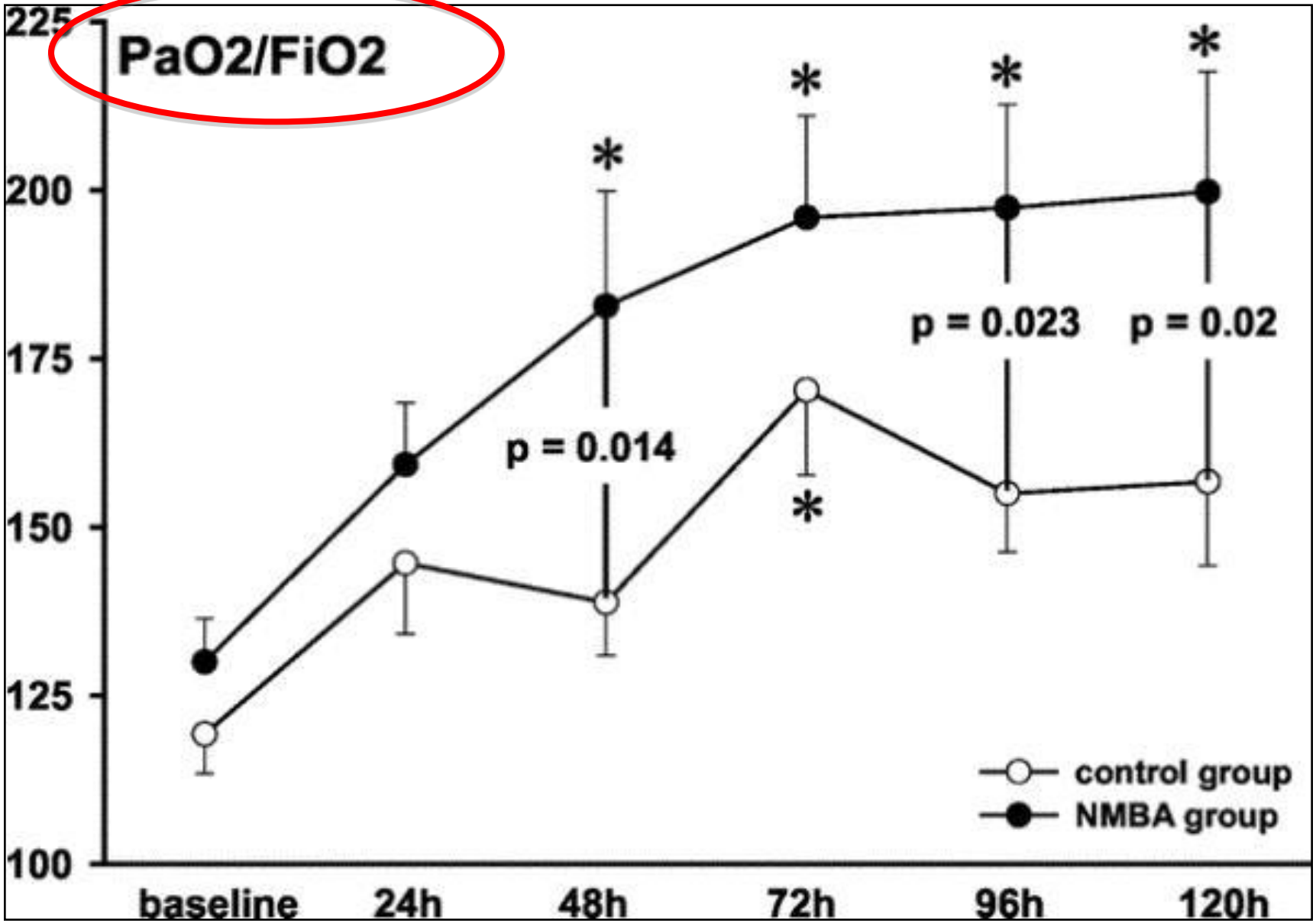
	NMBA Group (n = 28)	Control Group (n = 28)	*p* Value
Age, yrs	59.8 ± 17.5	61.5 ± 14.6	NS
Male, n (%)	21 (75)	20 (71)	NS
SAPS II	41.8 ± 10.4	45.4 ± 10.5	NS
Temperature, °C	37.7 ± 0.7	37.6 ± 0.6	NS
Cause of ARDS, n (%)			
Aspiration	7 (25)	7 (25)	NS
Community-acquired pneumonia	8 (28.6)	4 (14.3)	NS
Septic shock	3 (10.7)	3 (10.7)	NS
Pneumonia in immunocompromised	3 (10.7)	3 (10.7)	NS
Ventilator-associated pneumonia[a]	2 (7.1)	3 (10.7)	NS
Nosocomial pneumonia	2 (7.1)	2 (7.1)	NS
Lung contusion	1 (3.6)	2 (7.1)	NS
Peritonitis	1 (3.6)	2 (7.1)	NS
Miscellaneous	1 (3.6)	2 (7.1)	NS
Onset of ARDS, days	0.96 ± 0.79	1.14 ± 1.72	NS
Median (25th–75th percentiles)	1 (0–1)	1 (0–1)	NS
Pulmonary origin, n (%)	23 (82)	22 (79)	NS
Lung injury severity score, n (%)	2.89 ± 0.40	2.93 ± 0.42	NS
Days receiving mechanical ventilation	2.7 ± 2.6	3.4 ± 3.5	NS
Median (25th–75th percentiles)	2 (1–3.5)	2 (1–5.5)	NS

Gainnier. Crit Care Med 2004

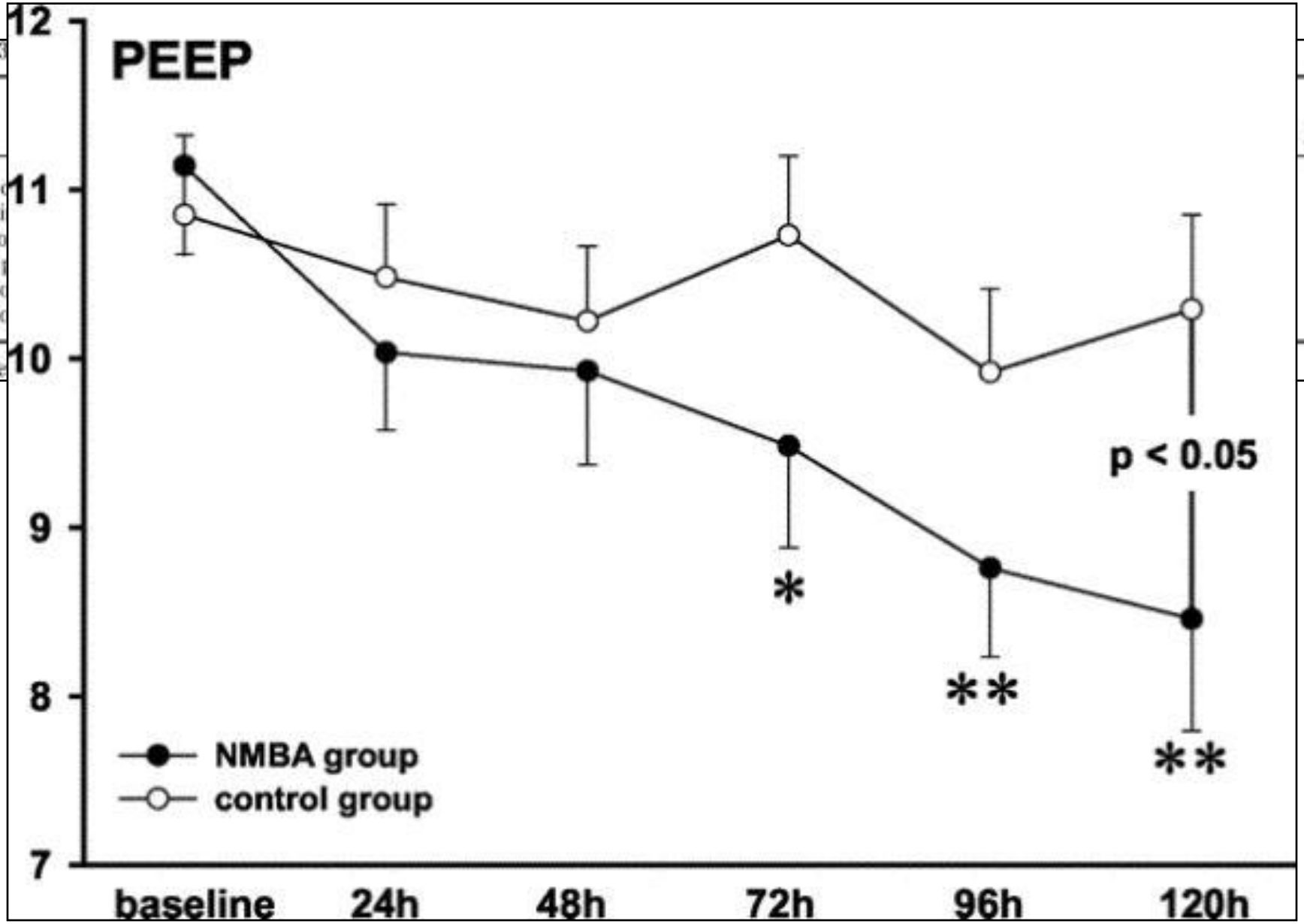
Table 2. Hemodynamic and respiratory parameters at inclusion

	NMBA Group (n = 28)	Control Group (n = 28)	*p* Value
Norepinephrine, n (%)	18 (64)	22 (79)	NS
Dobutamine, n (%)	8 (28.6)	5 (17.9)	NS
Pulmonary artery catheter, n (%)	6 (21.4)	5 (17.9)	NS
Heart rate, beats/min	99 ± 21	94 ± 24	NS
MAP, mm Hg	78 ± 11	75 ± 11	NS
CVP, mm Hg	9.6 ± 4.2	9.6 ± 5.5	NS
Hemoglobin, g/L	93.8 ± 17.7	101.5 ± 19.6	NS
Pao_2/Fio_2	130 ± 34	119 ± 31	NS
$Paco_2$, torr	48.3 ± 9.0	47.4 ± 11.2	NS
Fio_2	70.2 ± 17.0	67.3 ± 15.8	NS
PEEP, cm H_2O	11.1 ± 2.8	10.9 ± 2.4	NS
PEEPtot, cm H_2O	12.3 ± 3.0	11.4 ± 2.5	NS
Tidal volume, mL/kg	7.1 ± 1.1	7.4 ± 1.9	NS
Pplat, cm H_2O	27.1 ± 6.2	26.1 ± 4.0	NS
Pmean, cm H_2O	17.7 ± 3.3	17.2 ± 2.7	NS

Gainnier. Crit Care Med 2004



Gainnier. Crit Care Med 2004

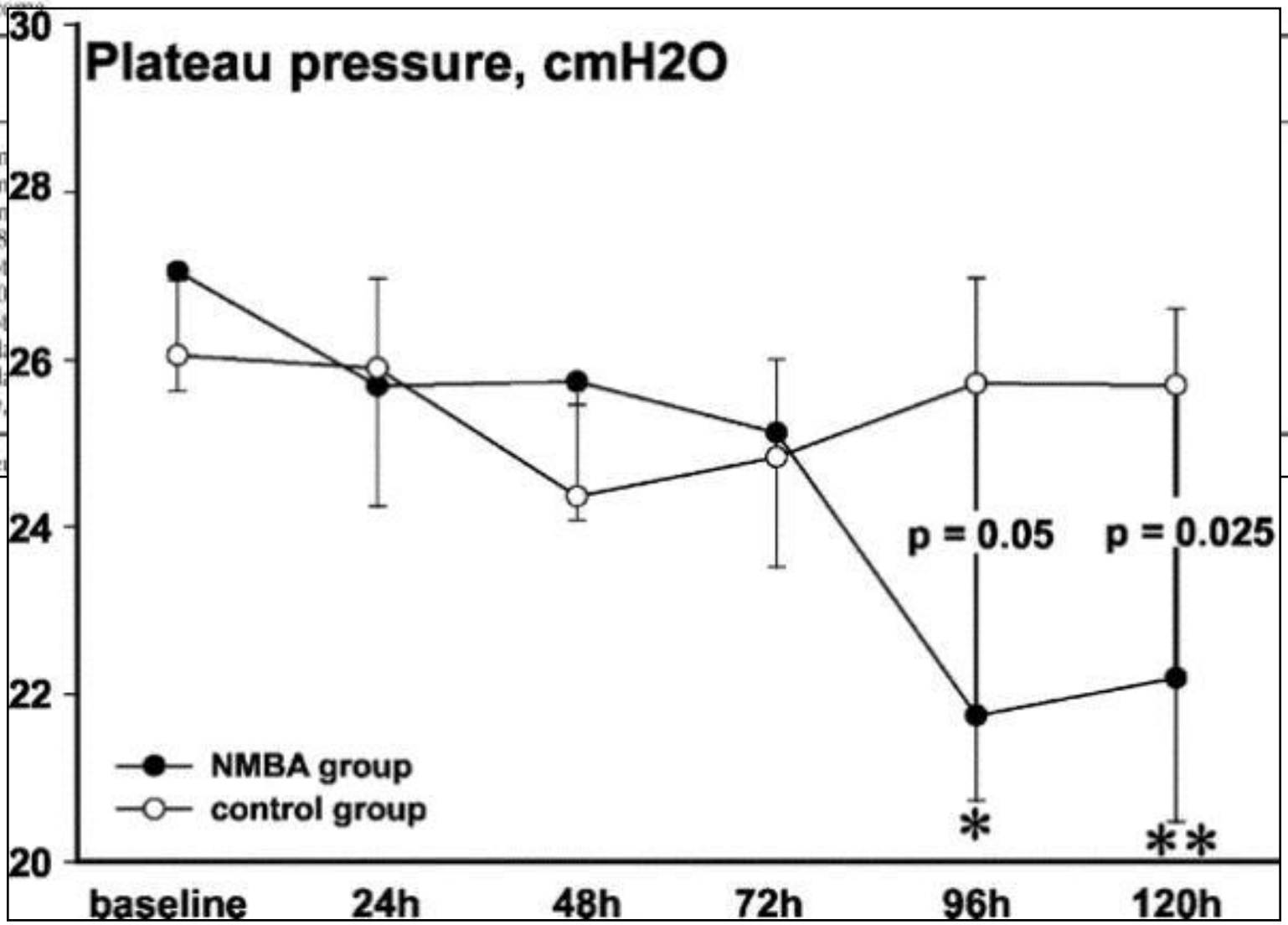


Gainnier. Crit Care Med 2004

Table 5. Outcome

	p Value
Duration of m	.94
Duration of m	.30
Duration of m	.76
VFD at day 28	.24
Median (25	.24
VFD at day 60	.071
Median (25	.11
Mortality at d	.061
Mortality at d	.18
ICU mortality,	.057

NMBA, ne



Gainnier. Crit Care Med 2004

The NEW ENGLAND JOURNAL of MEDICINE

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Neuromuscular Blockers in Early Acute Respiratory Distress Syndrome

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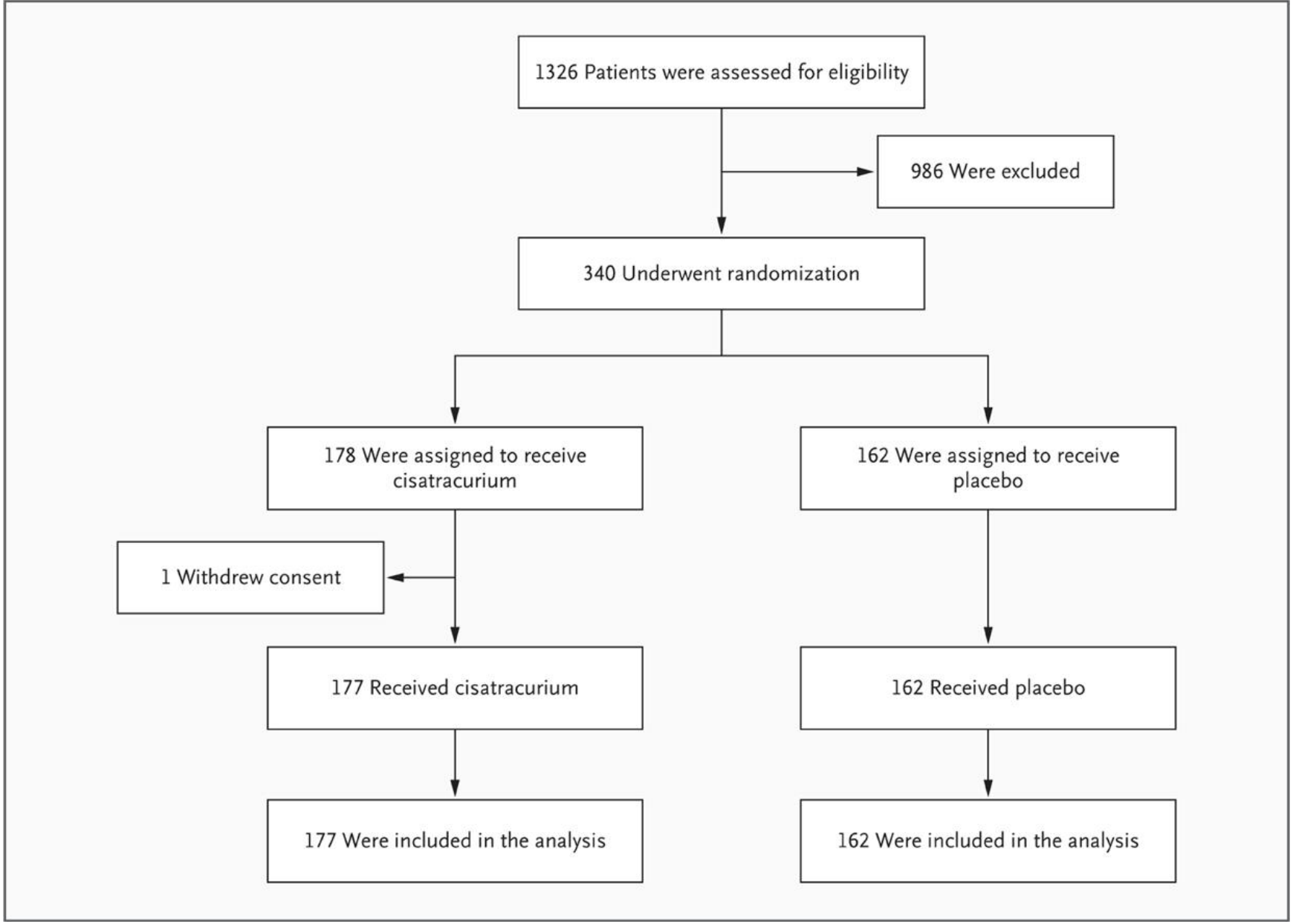
- Etude multicentrique, randomisée, double aveugle
- 340 pts SDRA sévère, PaO2/FiO2<150, PEEP>5 cm H2O, premières 48 heures, Vt 6-8 ml/kg
- Randomisation:
  - 178 pts, Gr. Cisatracurium, 48 heures
  - 162 pts, Gr. Placebo

- Crit. jugement principal: mortalité hospitalière et J 90.



Papazian *et al. N. Engl. J. Med.* 2010

Table 1. Summary of the Ventilation Procedure.*

Variable
Ventilator mode: volume assist–control
Initial tidal volume: 6–8 ml/kg of predicted body weight
Plateau pressure: ≤32 cm of water
Oxygenation goal: PaO_2 of 55–80 mm Hg or SpO_2 of 88–95%
Permitted combinations of FiO_2 and PEEP, respectively (cm of water): 0.3

Once the assigned Ramsay sedation score was 6 and the ventilator settings were adjusted, a 3-ml rapid intravenous infusion of 15 mg of cisatracurium besylate or placebo was administered, followed by a continuous infusion of 37.5 mg per hour for 48 hours.

[illegible] probably be futile, but permitted if the drug had its intended effect)
Procedure to correct hypercapnia when pH is <7.20 (in the following order, as needed): connect Y-piece directly to endotracheal tube, increase respiratory rate to a maximum of 35 cycles per min, and increase tidal volume to a maximum of 8 ml/kg
Weaning attempt: starting on day 3, if FiO_2 ≤0.6
Goals during weaning procedure: SpO_2 ≥88% and respiratory rate 26–35 cycles per min
Weaning procedure: decrease PEEP over 20–30 min to 5 cm of water
Pressure-support ventilation levels used during weaning procedure: 20, 15, 10, and 5 cm of water
If weaning procedure fails at a pressure-support ventilation level of 20 cm of water, switch to volume assist–control mode of ventilation
After at least 2 hr of successful pressure-support ventilation at a level of 5 cm of water, disconnect patient from the ventilator

Papazian *et al. N. Engl. J. Med.* 2010

Table 2. Baseline Characteristics of the Patients, According to Study Group.*

Characteristic†	Cisatracurium (N=177)	Placebo N=162)	P Value
Age — yr	58±16	58±15	0.70
Tidal volume — ml/kg of predicted body weight	6.55±1.12	6.48±0.92	0.52
Minute ventilation — liters/min	10.0±2.5	10.1±2.2	0.83
PEEP applied — cm of water	9.2±3.2	9.2±3.5	0.87
Plateau pressure — cm of water	25.0±5.1	24.4±4.7	0.32
Respiratory-system compliance — ml/cm of water	31.5±11.6	31.9±10.7	0.71
FIO_2	0.79±0.19	0.77±0.20	0.33
PaO_2:FIO_2‡	106±36	115±41	0.03
pH	7.31±0.10	7.32±0.10	0.11
PaO_2 — mm Hg	80±24	85±28	0.09
$PaCO_2$ — mm Hg	47±11	47±11	0.62
Prone position or inhaled nitric oxide or almitrine mesylate — no. (%)	33 (18.6)	23 (14.2)	0.31
SAPS II§	50±16	47±14	0.15
Nonfatal condition according to McCabe–Jackson score — no. (%)¶	133 (75.1)	125 (77.2)	0.66
Main reason for ICU admission — no. (%)			
Medical	129 (72.9)	113 (69.8)	0.52
Surgical, emergency	27 (15.3)	31 (19.1)	0.34
Surgical, scheduled	21 (11.9)	18 (11.1)	0.83
Corticosteroids for septic shock — no. (%)	70 (39.5)	73 (45.1)	0.30
Direct lung injury — no. (%)	142 (80.2)	123 (75.9)	0.34

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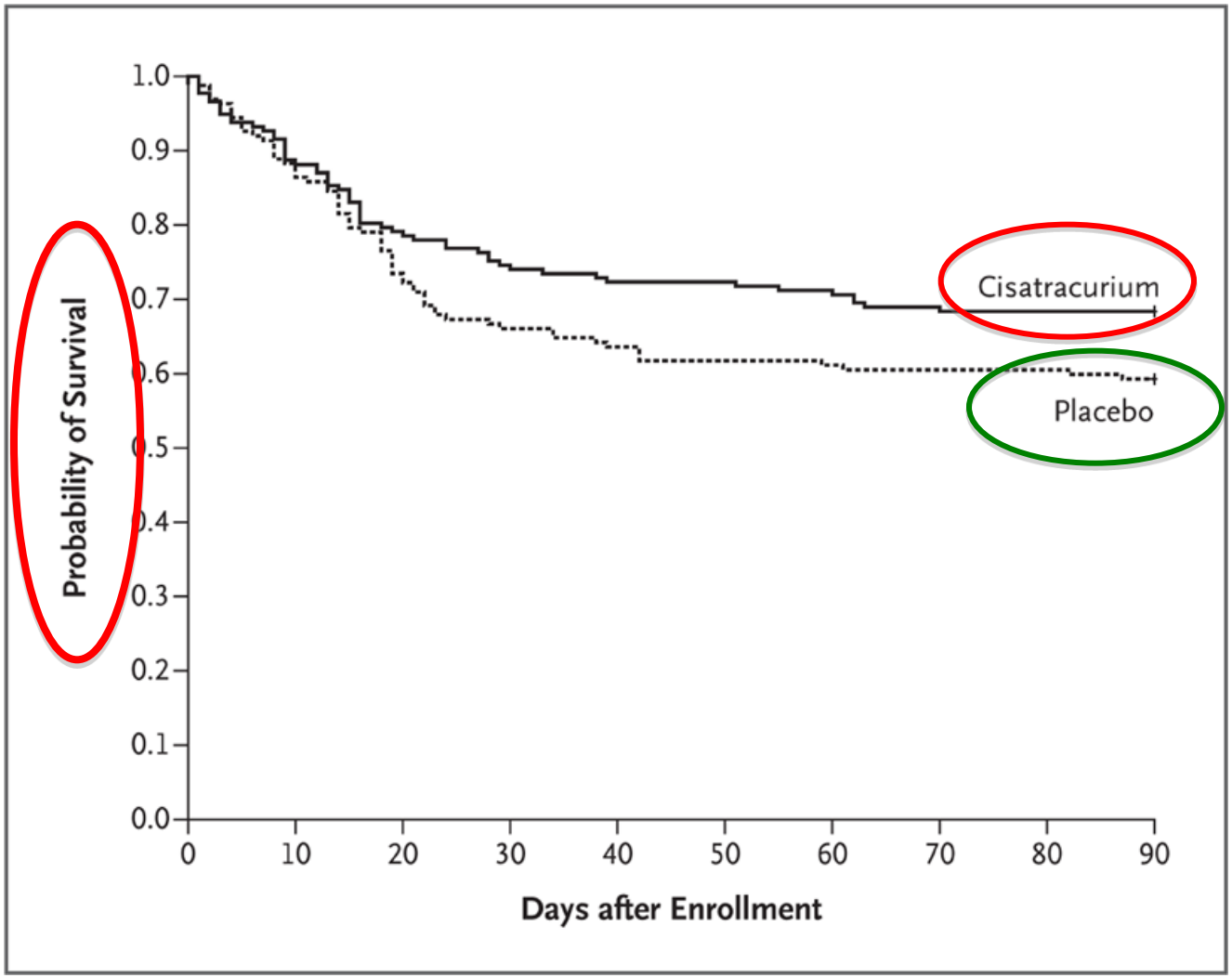

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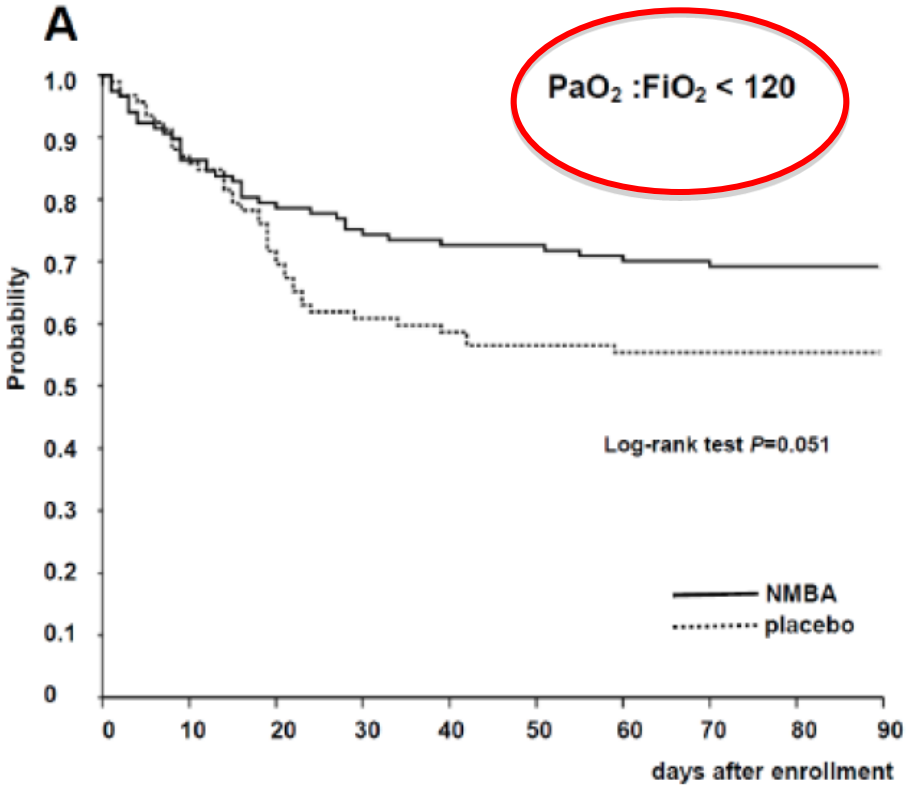
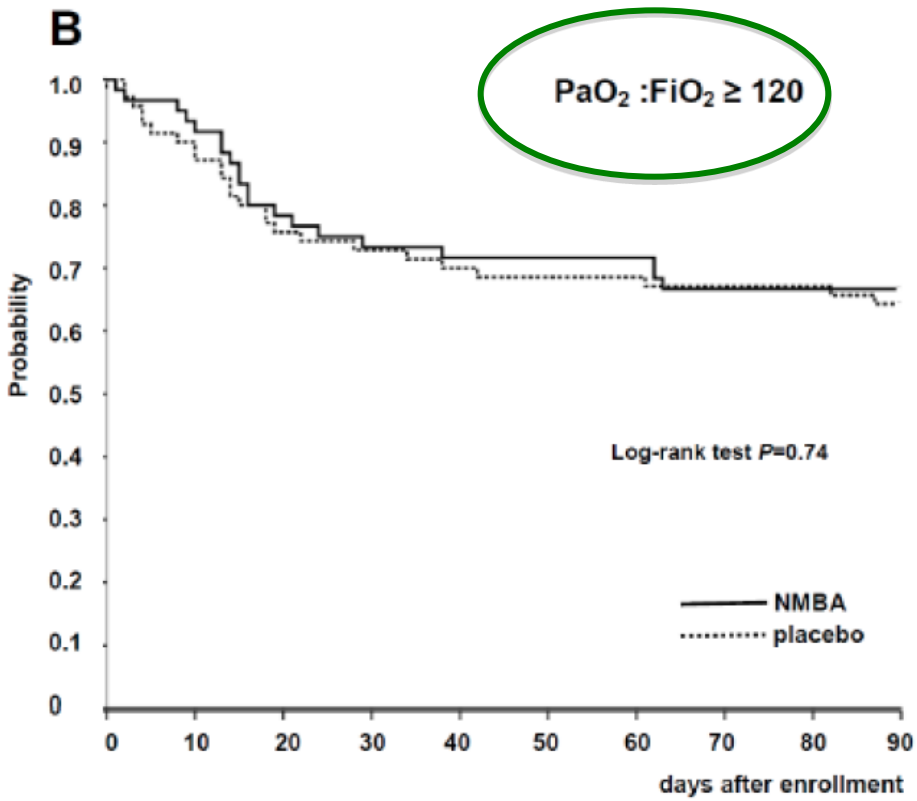




Papazian *et al. N. Engl. J. Med.* 2010

Table 3. Secondary Outcomes, According to Study Group.*

Outcome	Cisatracurium (N=177)	Placebo (N=162)	Relative Risk with Cisatracurium (95% CI)	P Value
Death — no. (% [95% CI])				
At 28 days	42 (23.7 [18.1–30.5])	54 (33.3 [26.5–40.9])	0.71 (0.51–1.00)	0.05

Chez des patients en ARDS sévère (PaO2/FiO2 <150 et surtout < 120), la curarisation précoce par cisatracurium améliore la survie à J 90, réduit la durée de la VM sans majorer le risque de neuromyopathies de réanimation.

From day 1 to day 28	6.9±8.2	5.7±7.8		0.16
From day 1 to day 90	47.7±33.5	39.5±35.6		0.03
Hospital survivors admitted to other health care facilities from day 1 to day 90 — % (95% CI)	22.3 (15.8–30.5)	18.8 (12.2–27.8)		0.52
Barotrauma — no. (% [95% CI])‡	9 (5.1 [2.7–9.4])	19 (11.7 [7.6–17.6])	0.43 (0.20–0.93)	0.03
Pneumothorax — no. (% [95% CI])	7 (4.0 [2.0–8.0])	19 (11.7 [7.6–17.6])	0.34 (0.15–0.78)	0.01
MRC score — median (IQR)§				
At day 28	55 (46–60)	55 (39–60)	1.07 (0.80–1.45)	0.49
At ICU discharge	55 (43–60)	55 (44–60)	0.92 (0.71–1.19)	0.94
Patients without ICU-acquired paresis¶				
By day 28 — no./total no. (% [95% CI])	68/96 (70.8 [61.1–79.0])	52/77 (67.5 [56.5–77.0])		0.64
By ICU discharge — no./total no. (% [95% CI])	72/112 (64.3 [55.1–72.6])	61/89 (68.5 [58.3–77.3])		0.51

Papazian *et al. N. Engl. J. Med.* 2010

Neuromuscular blocking agents in patients with acute respiratory distress syndrome: a summary of the current evidence from three randomized controlled trials

Annals of Intensive Care

Annals of Intensive Care 2012, **2**:33

Ary Serpa Neto[1*], Victor Galvão Moura Pereira[1], Daniel Crepaldi Espósito[1], Maria Cecília Toledo Damasceno[1] and Marcus J Schultz[2]

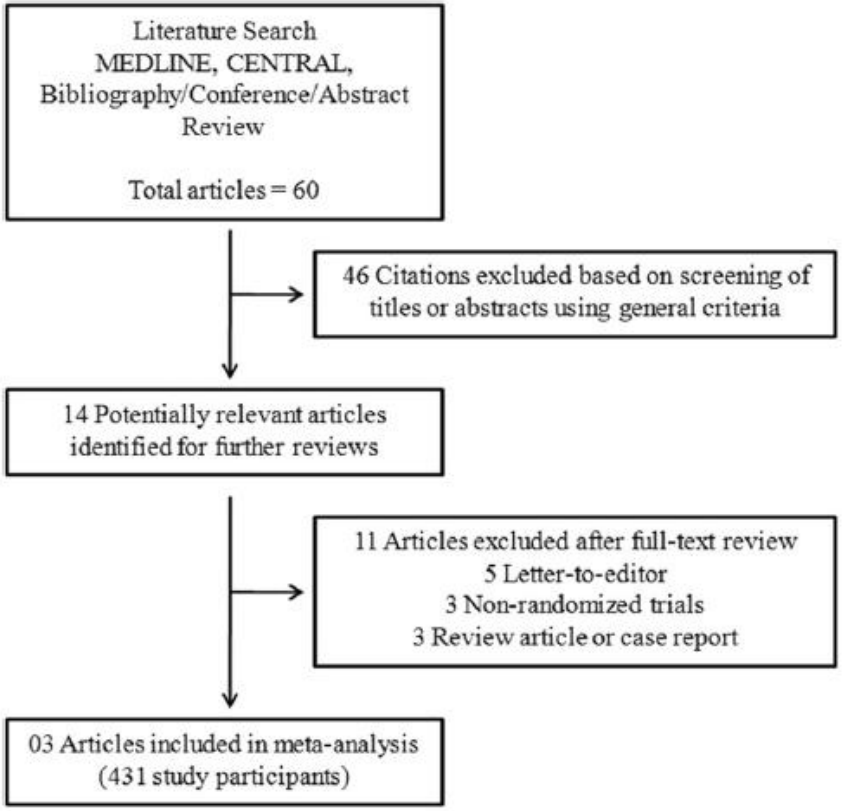


Figure 1 Literature search strategy.

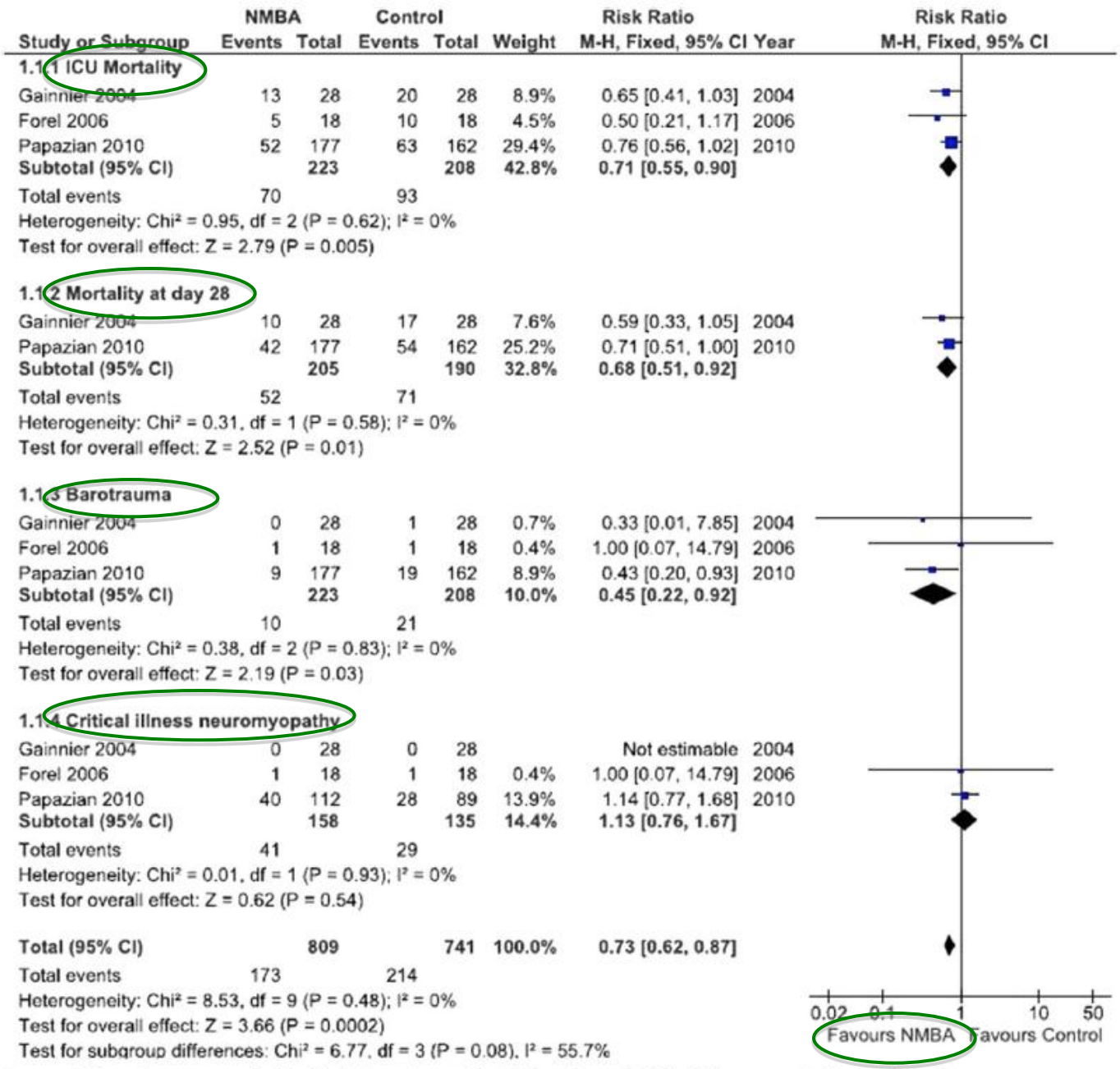


Figure 2 Effect of neuromuscular blockade in patients with ARDS at the end of the follow-up period for each study.

	T0		T72		Change in Cisatracurium	Change in Control	p value
	Cisatracurium (n = 223)	Control (n = 208)	Cisatracurium (n = 223)	Control (n = 208)			
PaO_2 / FiO_2	113.6 ± 14.1	119.6 ± 5.03	197.3 ± 32.0	165.6 ± 7.50	83.66 ± 35.92	46.00 ± 4.58	0.050
$PaCO_2$, mmHg	48.80 ± 2.09	47.20 ± 0.20	45.43 ± 1.35	44.76 ± 1.59	- 3.36 ± 1.97	- 2.43 ± 1.43	0.658
PEEP, cmH_2O	11.16 ± 2.00	10.36 ± 1.01	10.10 ± 0.81	10.50 ± 0.75	- 1.06 ± 1.22	0.13 ± 0.47	0.127
V_T, mL/kg	6.71 ± 0.33	6.96 ± 0.46	6.80 ± 0.34	7.00 ± 0.45	0.08 ± 0.02	0.04 ± 0.05	0.246
FiO_2, %	76.40 ± 5.39	71.76 ± 4.89	56.00 ± 1.00	59.00 ± 0.00	- 20.40 ± 5.57	- 12.76 ± 4.8	0.127

Effet bénéfique des curares lors d'une utilisation précoce dans le SDRA, sans majoration des neuromyopathies de réanimation.

Prudence: les études évaluées provenaient du même groupe de travail.

Neto *et al. Annals of Intensive Care* 2012

Neuromuscular blocking agents in acute respiratory distress syndrome: a systematic review and meta-analysis of randomized controlled trials

CRITICAL CARE

Critical Care 2013, 17:R43

Waleed Alhazzani[1*], Mohamed Alshahrani[2], Roman Jaeschke[1,3], Jean Marie Forel[4], Laurent Papazian[4], Jonathan Sevransky[5] and Maureen O Meade[1,3]

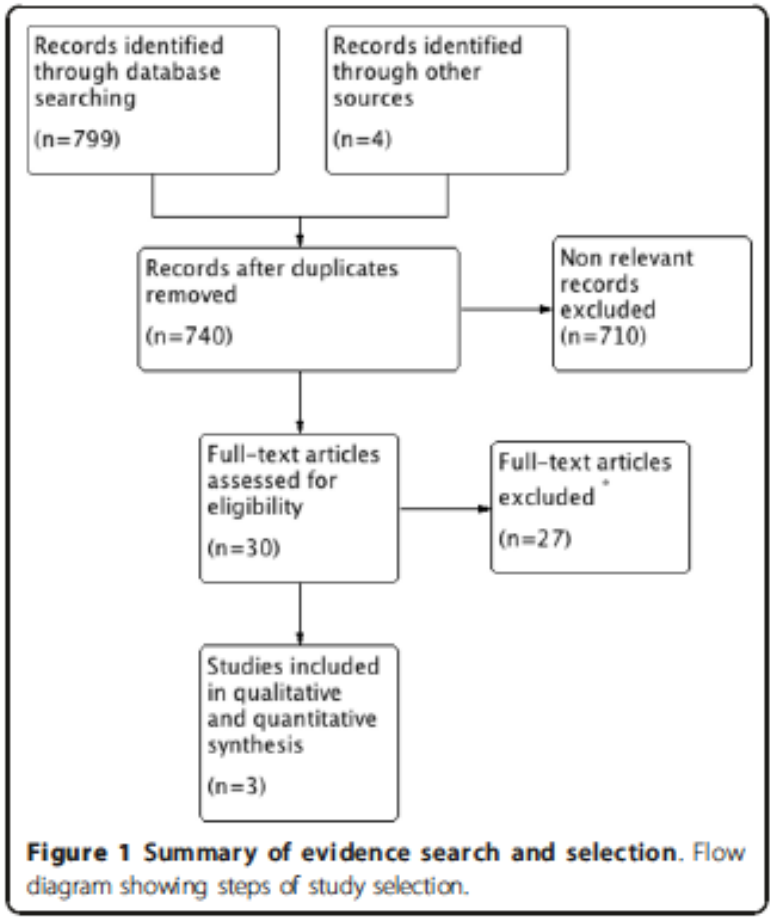


Figure 1 Summary of evidence search and selection. Flow diagram showing steps of study selection.

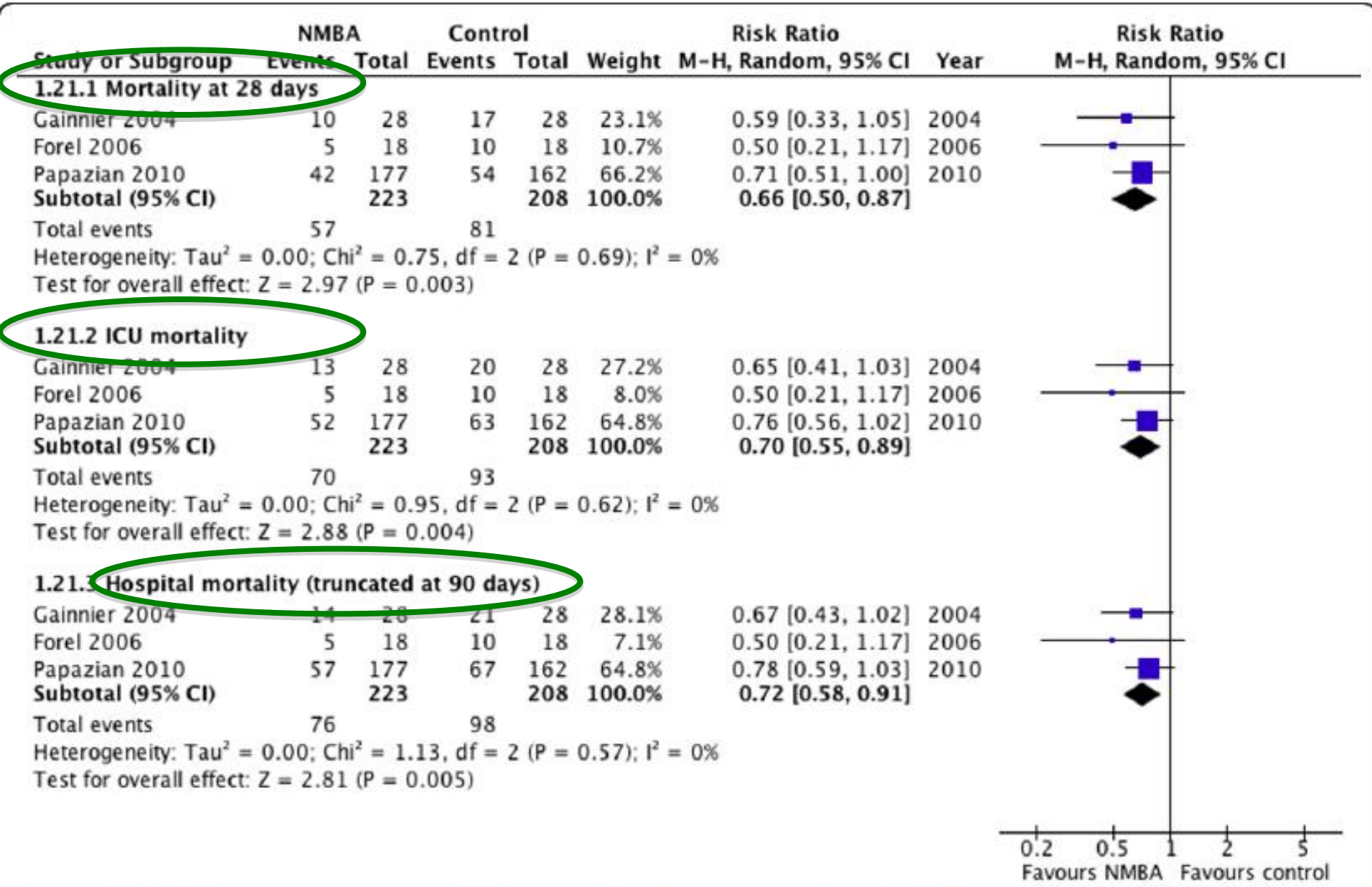


Figure 2 Mortality. Forest plot comparing neuromuscular blockers and placebo for the following outcomes: 28 days, ICU, and hospital (truncated at 90 days), results are shown by using random-effects model with relative risk and 95% confidence interval

Study or Subgroup	Cisatracurium Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Random, 95% CI	Year
Gainnier 2004	0	28	1	28	5.5%	0.33 [0.01, 7.85]	2004
Forel 2006	0	18	0	18		Not estimable	2006
Papazian 2010	9	177	19	162	94.5%	0.43 [0.20, 0.93]	2010
Total (95% CI)		**223**		**208**	**100.0%**	**0.43 [0.20, 0.90]**	
Total events	9		20				

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.03$, df = 1 (P = 0.87); $I^2 = 0\%$

Test for overall effect: Z = 2.24 (P = 0.02)

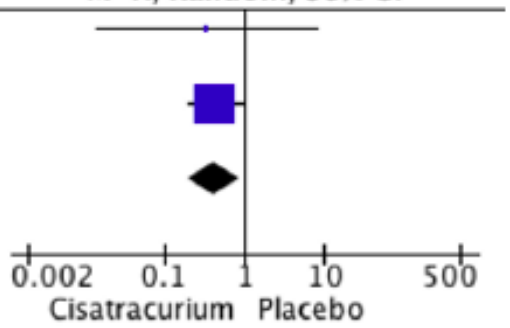


Figure 3 Barotrauma. Forest plot comparing neuromuscular blockers and placebo for barotrauma outcome; results are shown by using random-effects model with relative risk and 95% confidence interval.

Barotraumatismes

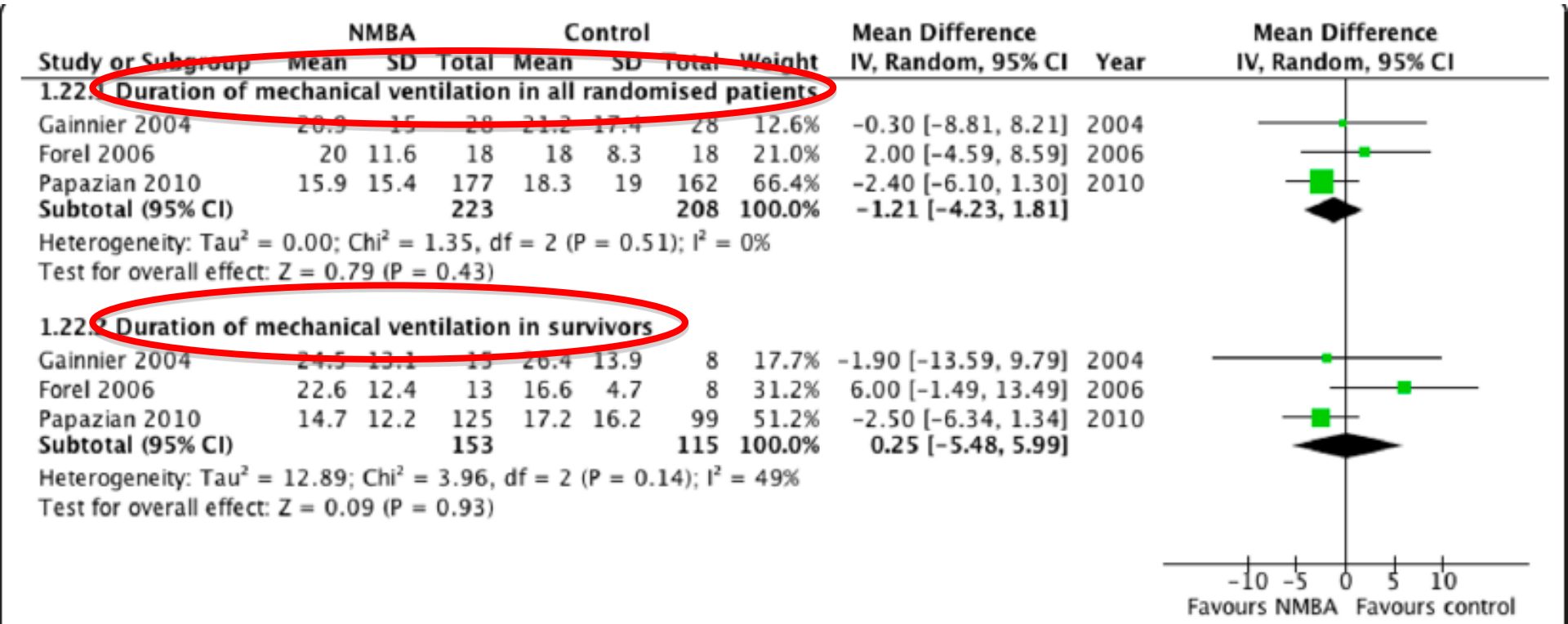


Figure 4 Duration of mechanical ventilation. Forest plot comparing neuromuscular blockers and placebo for the duration of mechanical ventilation in all patients and in survivors; results are shown by using random-effects model with relative risk and 95% confidence interval.

Study or Subgroup	Cisatracurium Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Random, 95% CI	Year
Gainnier 2004	0	28	0	28		Not estimable	2004
Forel 2006	1	18	1	18	1.0%	1.00 [0.07, 14.79]	2006
Papazian 2010	72	177	61	162	99.0%	1.08 [0.83, 1.41]	2010
Total (95% CI)		**223**		**208**	**100.0%**	**1.08 [0.83, 1.41]**	
Total events	73		62				

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.00$, df = 1 ($P = 0.96$); $I^2 = 0\%$
Test for overall effect: $Z = 0.57$ ($P = 0.57$)

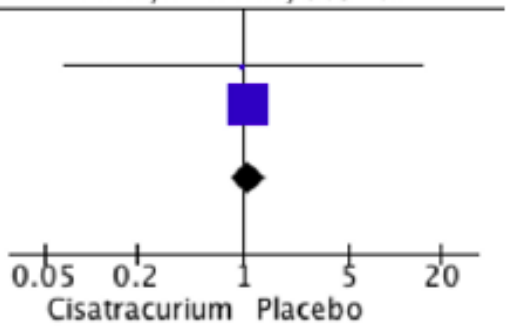


Figure 5 ICU-acquired weakness. Forest plot comparing neuromuscular blockers and placebo for ICU-acquired weakness outcome; results are shown by using random-effects model with mean difference and 95% confidence interval.

Neuromyopathies de réanimation

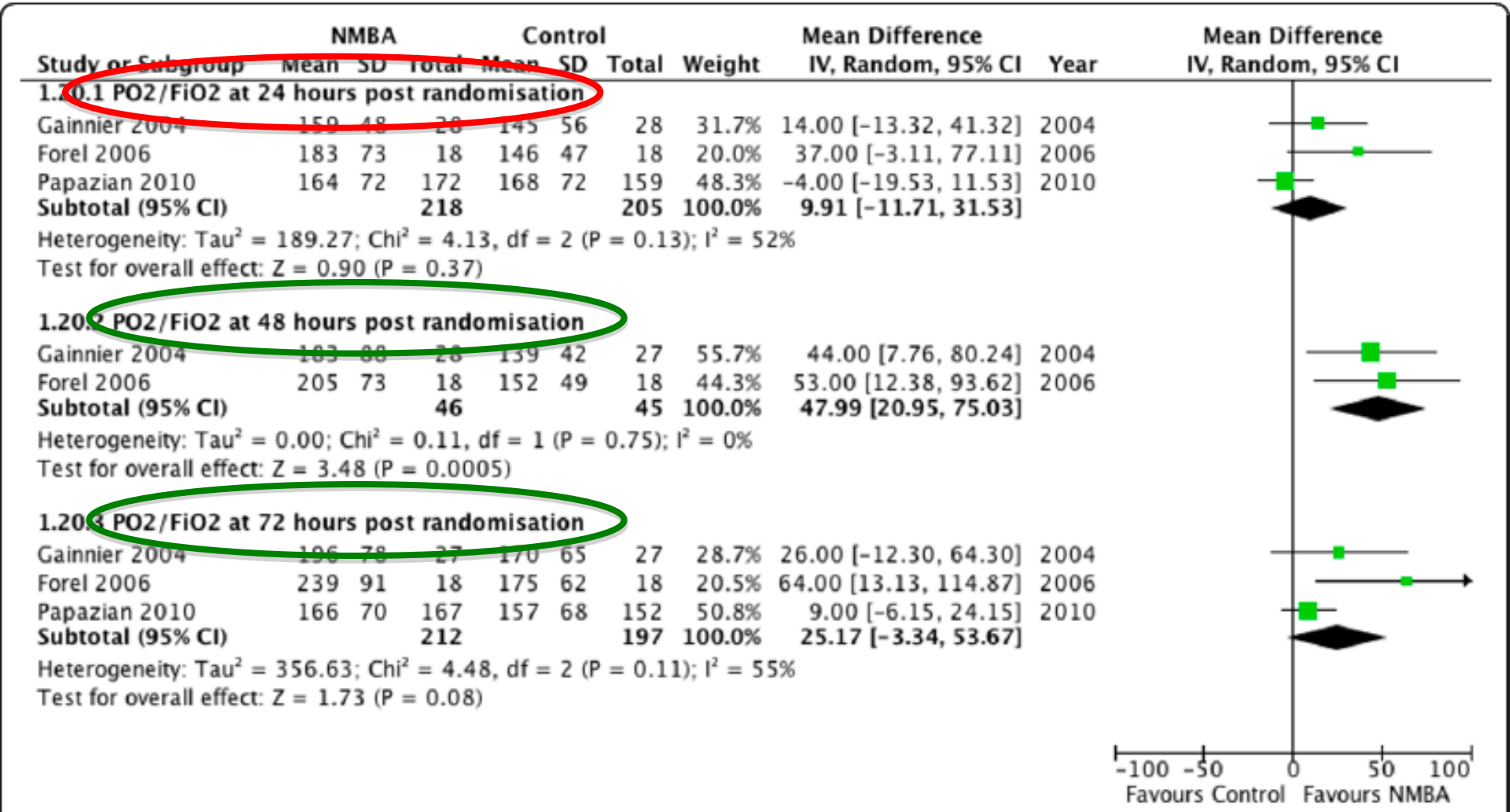


Figure 6 Oxygenation at 24 to 72 hours. Forest plot comparing neuromuscular blockers and placebo for oxygenation outcome (measured by using PaO_2/FiO_2 at 24 to 72 hours after randomization); results are shown by using random-effects model with mean difference and 95% confidence interval.

En résumé

- Quel que soit le mode de VM dans le SDRA sévère
  - ➢ Protection parenchyme pulmonaire fondamentale
  - ➢ Abolition complète de la VS par la curarisation pour une durée de 48 h améliore la survie.
  - ➢ Courte durée d'utilisation : faible incidence neuromyopathies.

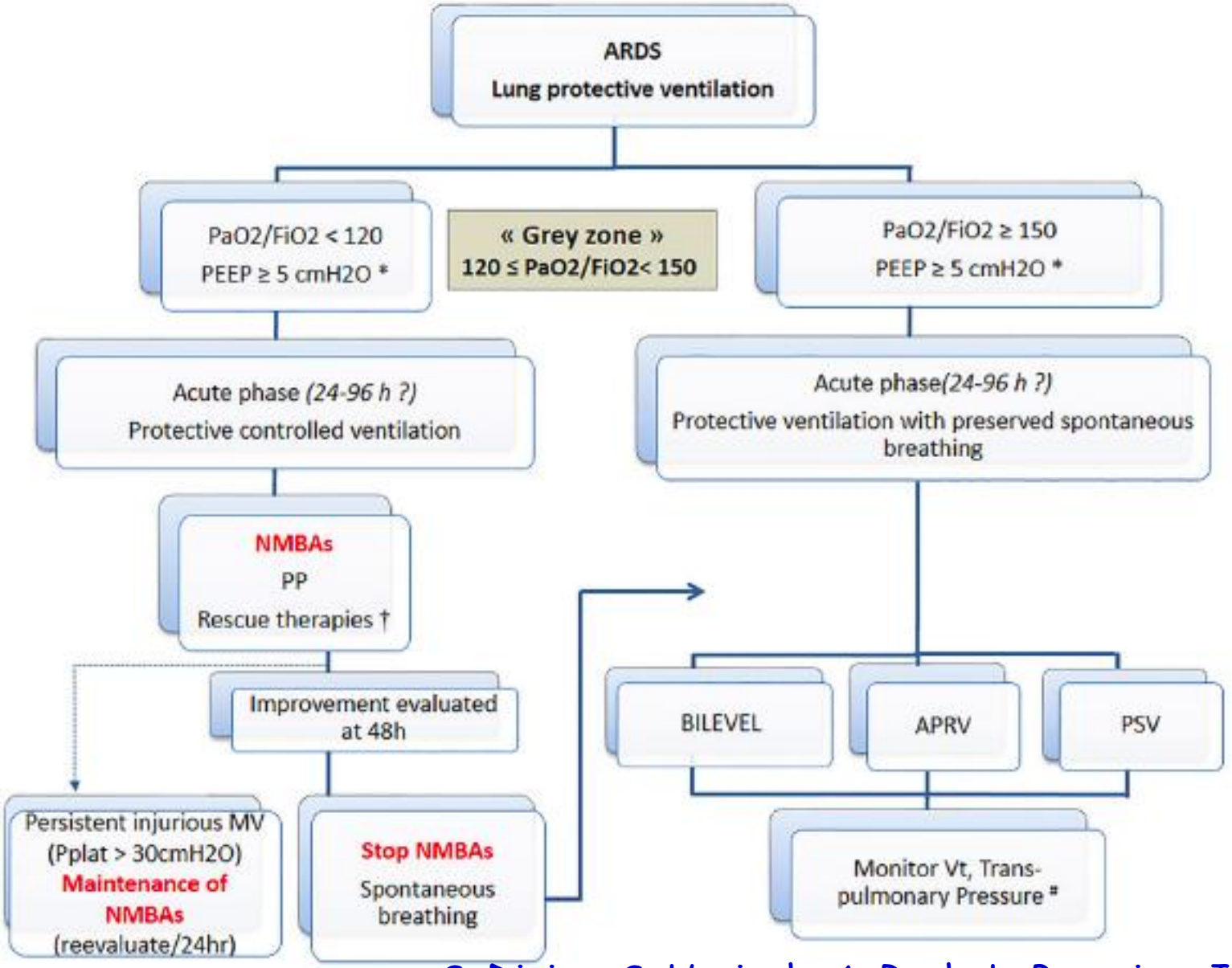
- Utilisation précoce et limitée des curares:
  - ✓ Nécessite sédation profonde
  - ✓ Limitation VS pendant la phase la plus à risque de complications parenchymateuses

En résumé

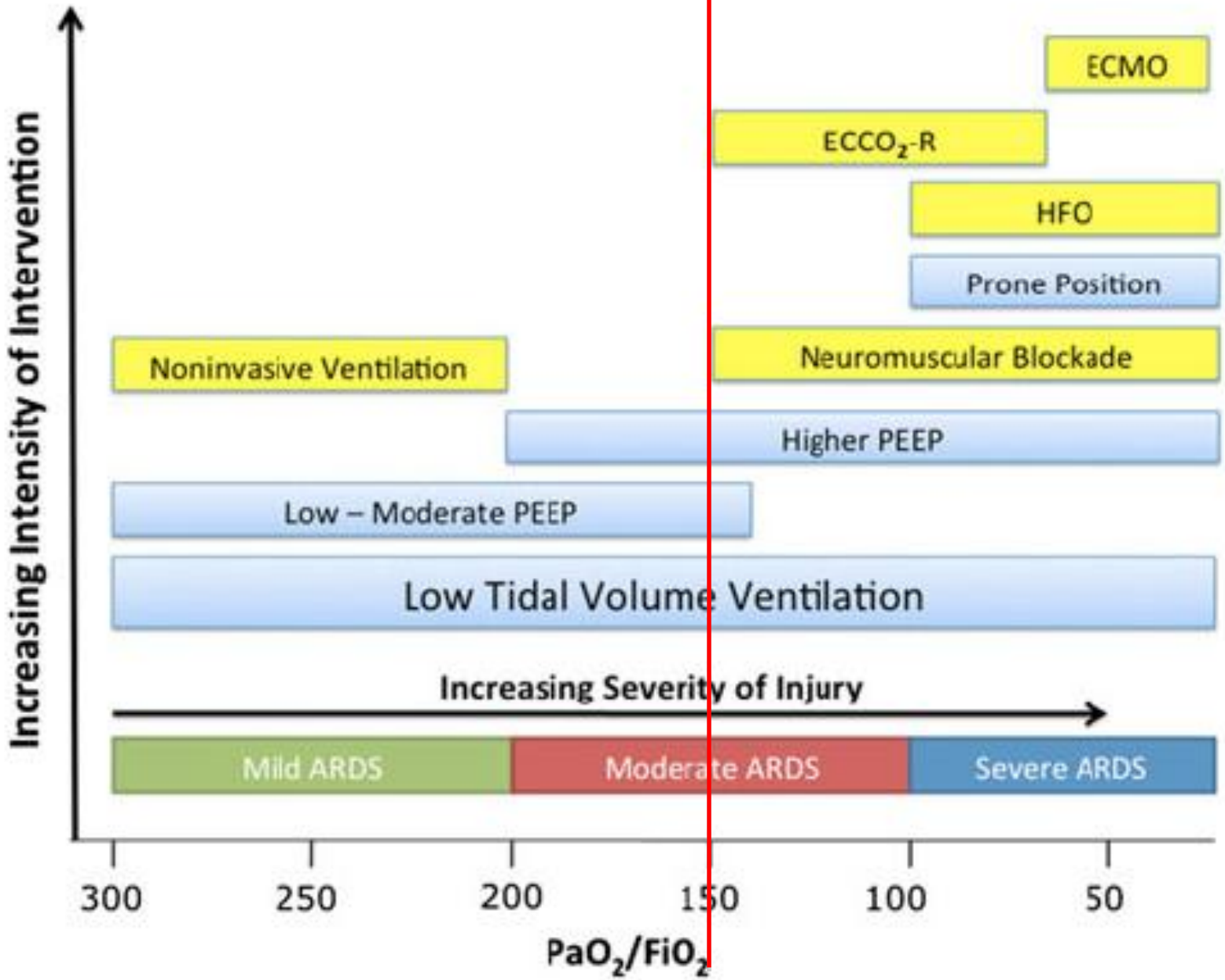
- Abolition de la ventilation spontanée à la phase initiale
  - +++ processus inflammatoires et biotraumatiques
  - impact positif sur survie patients les plus hypoxémiques.

- Maintien ventilation spontanée
  - SDRA légers ou modérés (P/F>150)
  - Titration ou réévaluation de la sédation
  - Sédation de « confort ».

En résumé



S. Dizier, S. Hraiech, A. Roch, L. Papazian, JEPU 2015



Intensive Care Med (2012) 38:1573–1582

JAMA. 2012;307(23):2526-2533

Conclusion

- Curarisation lors du SDRA longtemps controversée.

- Essais randomisés contrôlés récents
  - Prise en charge des SDRA à la phase précoce.
  - Effet positif démontré dans le SDRA sévère où la ventilation spontanée peut être délétère.
  - Durée utilisation courte non associée à une augmentation des neuromyopathies acquises en réanimation

- SDRA léger ou modéré: VS, sédation de confort