CON: Neuromuscular blockade should not be used routinely in ARDS management

David Willms, MD FCCP FCCM
San Diego, California

1

ACURASYS Trial

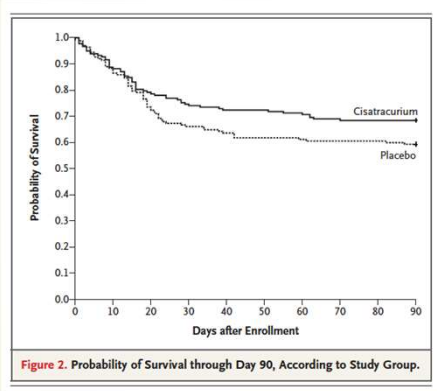


Figure 2. Probability of Survival through Day 90, According to Study Group.

- Early ARDS, PRCT, *n* = 340
- P/F < 150, PEEP ≥ 5
- Fixed dose x 48 hr (cisatra only)
- + Δ 90 d adjusted mortality (p=0.04) – (only with P/F < 120)
- No change crude 90 d mortality
- Less barotrauma
- No Δ ICU muscle weakness

Papazian et al *N Eng J Med* 2010; 363:1107

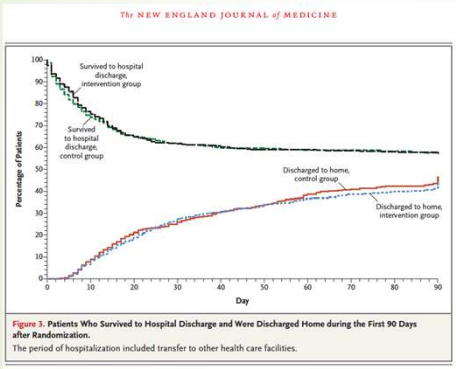
2

- "In conclusion, this multicenter trial provides evidence that the administration of a neuromuscular blocking agent early in the course of severe ARDS managed with low tidal-volume ventilation may improve outcomes. Further studies are needed to replicate and expand these findings before they can be widely adopted in clinical practice."

Papazian et al *N Eng J Med* 2010; 363:1107

3

ROSE Trial



- Similar protocol to ACURASYS
- P/F < 150, PEEP ≥ 8, *n* =1006
- Stopped early for futility
- No Δ 90 day mortality
- No Δ secondary endpoints
- More CV complications
- Control group less sedated

PETAL Network *N Engl J Med* 2019; 380:21

4

Potential for Adverse Effects

- Neuromuscular weakness
- DVT risk
- Paralysis awareness
- Anaphylaxis
- Adverse cardiovascular events
- ? VAP, skin breakdown

5

Neuromuscular Blocking Agents and Neuromuscular Dysfunction Acquired in Critical Illness: A Systematic Review and Meta-Analysis

David R. Price, MD[1,3]; Mark E. Mikkelsen, MD, MSCE[2,3]; Craig A. Umscheid, MD, MSCE[1,3]; Ehrin J. Armstrong, MD, MSc[4,5]

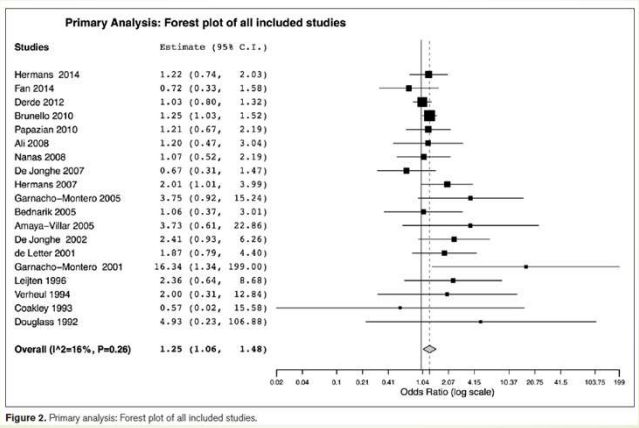


Figure 2. Primary analysis: Forest plot of all included studies.

Crit Care Med 2016; 44:2070

6

DVT Risk

Table 2 Univariate analysis of baseline and time-dependent risk factors for DVT incidence in the ICU during the prospective phase

	No DVT (n = 245). Frequency (%) or median (25th–75th percentile)	DVT (n = 12). Frequency (%) or median (25th–75th percentile)	P (Mann–Whitney U) or Fisher's exact test
Gender M/F	167/78 (68.2/31.8%)	8/4 (66.7/33.3%)	1
Age (years)	53 (35–72)	61 (46.5–77.5)	0.289
Body weight (kg)	75 (65–80)	72.5 (70–78)	0.906
Height (cm)	172 (165–178)	171 (162–175)	0.464
Systolic blood pressure (mmHg)	120 (100–130)	120 (110–130)	0.987
Glasgow coma scale	11 (6–15)	11 (5–14)	0.718
SAPS II	41 (26–55)	40 (32–57)	0.979
Length of mechanical ventilation (days)	3 (1–9)	14.5 (6.5–19.75)	0.001
CVVH	16 (6.6%)	2 (16.7%)	0.206
Family history of DVT	2 (0.8%)	0 (0%)	1
Chronic illness	46 (18.8%)	4 (33.3%)	0.257
Bacteriemia	39 (16.0%)	1 (8.3%)	0.698
D-dimer positivity	184 (75.1%)	12 (100%)	0.075
Mioglobin positivity	135 (55.1%)	10 (83.3%)	0.073
Troponine I positivity	87 (35.5%)	5 (41.7%)	0.760
Mechanical measures of prophylaxis	155 (63.3%)	10 (83.3%)	0.222
Xigris/Ceprotin	12 (4.9%)	1 (8.3%)	0.474
Heparin	26 (10.6%)	2 (16.7%)	0.626
Acetylsalicylic acid	24 (9.8%)	1 (8.3%)	1
Catecholamines	142 (58.0%)	11 (91.7%)	0.031
Sedatives	221 (86.1%)	11 (91.7%)	1
Diprivan	187 (76.3%)	11 (91.7%)	0.307
Ipnovel	107 (43.7%)	8 (66.7%)	0.143
Fentanyl	158 (64.5%)	10 (83.3%)	0.227
Morphine	144 (59.0%)	5 (41.7%)	0.248
Neuromuscular block	99 (40.4%)	10 (83.3%)	0.005
Drugs adverse reactions	12 (4.9%)	2 (16.7%)	0.133
LMWH	236 (96.3%)	11 (91.7%)	0.386
AT III (%)	72 (55–86)	59 (49–78)	0.122
PT (%)	70 (58–88)	69 (56–97)	0.649
PTT (s)	29.9 (26.7–34.1)	29.5 (25.7–31.9)	0.586
RBC transfusion (units)	2 (0–4)	4 (0–10)	0.105
Plasma transfusion (units)	0 (0–4)	4 (0–7)	0.060
PLT transfusion	44 (18.0%)	2 (16.7%)	1

Boddi et al *J Thromb Haemostasis* 2009; 8:121

7

Meta-Analysis > Crit Care Med. 2021 Mar 1;49(3):e304-e314.
doi: 10.1097/CCM.0000000000004824.

Awareness With Paralysis in Mechanically Ventilated Patients in the Emergency Department and ICU: A Systematic Review and Meta-Analysis

Ryan D Pappal [1], Brian W Roberts [2], Winston Winkler [1], Lauren H Yaegar [3], Robert J Stephens [4], Brian M Fuller [4 5]

Affiliations + expand

PMID: 33566462 PMCID: PMC7902430 DOI: 10.1097/CCM.0000000000004824

- ~ 0.1% reported during surgical procedures in OR
- 1.9 – 3.4% in this meta-analysis in ER/ICU
- Probably under-reported

8

What does *UpToDate* Say?

"We suggest **not routinely** administering neuromuscular blockers (NMBs) to patients with ARDS. This approach is based upon a lack of robust evidence to support meaningful benefit in patients with ARDS and the potential for harm. While data are limited, we reserve their use for a limited number patients with ARDS who have severe hypoxemia refractory to standard therapies and patients with severe ventilator dyssynchrony that is refractory to ventilator adjustment and sedation, particularly if it leads to double triggering…"

Siegel, Siemieniuk *UpToDate* 3/28/23

9

CONFERENCE REPORTS AND EXPERT PANEL

ESICM guidelines on acute respiratory distress syndrome: definition, phenotyping and respiratory support strategies

Giacomo Grasselli[1,2*], Carolyn S. Calfee[3], Luigi Camporota[4,5], Daniele Poole[6], Marcelo B. P. Amato[7], Massimo Antonelli[8,9], Yaseen M. Arabi[10,11,12], Francesca Baroncelli[13], Jeremy R. Beitler[14], Giacomo Bellani[15,16], Geoff Bellingan[17], Bronagh Blackwood[18], Lieuwe D. J. Bos[19], Laurent Brochard[20,21], Daniel Brodie[22], Karen E. A. Burns[21,23,24,25], Alain Combes[26,27], Sonia D'Arrigo[8], Daniel De Backer[28], Alexandre Demoule[29,30], Sharon Einav[31], Eddy Fan[21], Niall D. Ferguson[32,33], Jean-Pierre Frat[34,35], Luciano Gattinoni[36], Claude Guérin[37,38], Margaret S. Herridge[39], Carol Hodgson[40,41], Catherine L. Hough[42], Samir Jaber[43], Nicole P. Juffermans[44], Christian Karagiannidis[45], Jozef Kesecioglu[46], Arthur Kwizera[47], John G. Laffey[48,49], Jordi Mancebo[50], Michael A. Matthay[51], Daniel F. McAuley[18,52], Alain Mercat[53], Nuala J. Meyer[54], Marc Moss[55], Laveena Munshi[56], Sheila N. Myatra[57], Michelle Ng Gong[58,59], Laurent Papazian[60,61], Bhakti K. Patel[62], Mariangela Pellegrini[63], Anders Perner[64], Antonio Pesenti[1,2], Lise Piquilloud[65], Haibo Qiu[66], Marco V. Ranieri[67,68], Elisabeth Riviello[69], Arthur S. Slutsky[21,24], Renee D. Stapleton[70], Charlotte Summers[71], Taylor B. Thompson[72], Carmen S. Valente Barbas[73,74], Jesús Villar[24,75,76], Lorraine B. Ware[77], Björn Weiss[78], Fernando G. Zampieri[79,80], Elie Azoulay[81] and Maurizio Cecconi[82,83] on behalf of the European Society of Intensive Care Medicine Taskforce on ARDS

Recommendation 8.1

We **recommend against** the *routine* use of continuous infusions of NMBA to reduce mortality in patients with moderate-to-severe ARDS not due to COVID-19.
Strong recommendation, moderate level of evidence.

We are **unable to make a recommendation** for or against the *routine* use of continuous infusions of NMBA to reduce mortality in patients with moderate-to-severe ARDS due to COVID-19.
No recommendation; no evidence.

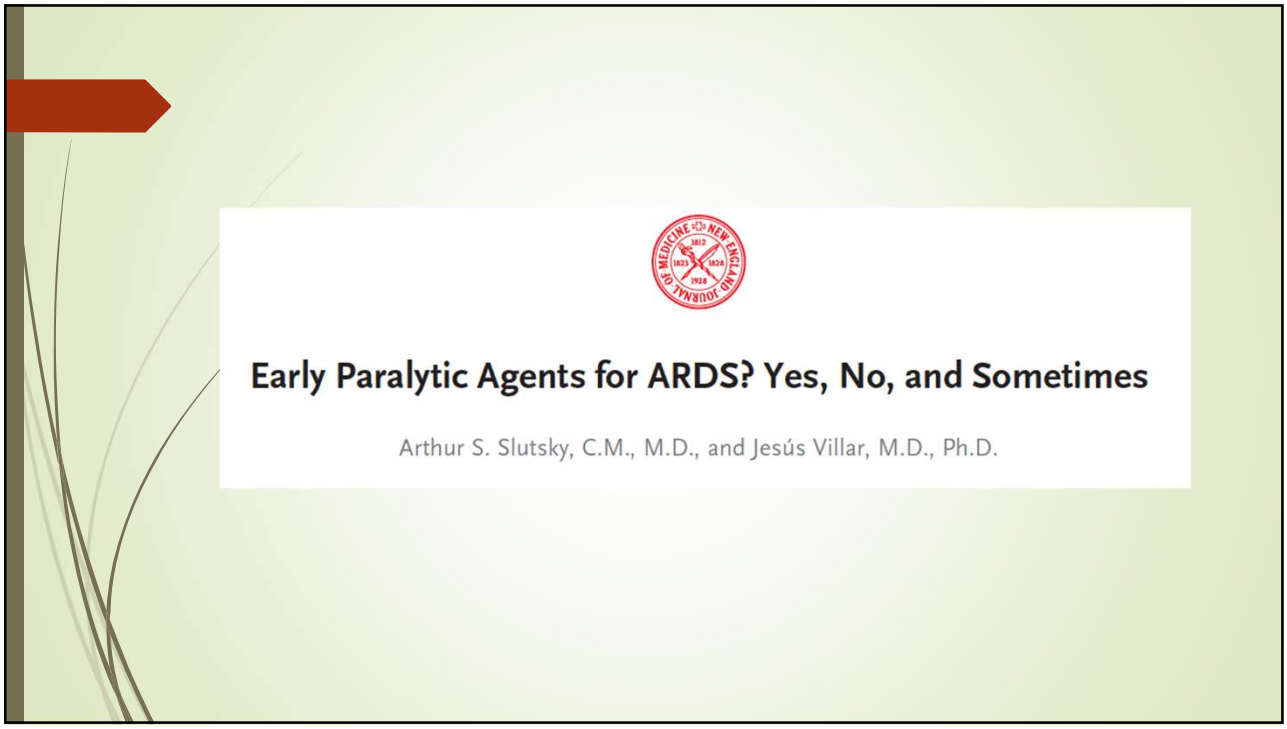
Intensive Care Med 2023; 49:727

10

Why not routinely paralyze patients on ventilators with ARDS

- No proven effect on outcomes of interest
- Requires deep sedation, itself associated with adverse outcomes
- May increase risk of
  - VAP
  - VTE
  - Neuromuscular weakness
  - Anaphylaxis
  - Decubiti
  - Adverse CV events
- Lose benefits of spontaneous ventilatory effort
- Potential for awareness under paralysis, and PTSD
- Sometimes a tendency to continue too long

11



12