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Original Research Article

# EARLY NEUROMUSCULAR BLOCKADE VERSUS LUNG-PROTECTIVE VENTILATION ALONE IN MODERATE-TO-SEVERE ARDS: A RANDOMIZED CONTROLLED TRIAL

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## ABSTRACT

**Background:** Neuromuscular blockade (NMB) may improve outcomes in ARDS by reducing ventilator-induced lung injury. **Objective:** To compare early NMB with LPV alone in patients with moderate-to-severe ARDS. **Materials and Methods:** A randomized controlled trial was conducted with 100 patients (50 per group). Primary outcome was 28-day mortality. Secondary outcomes included ventilator-free days, ICU length of stay, and incidence of barotrauma. **Results:** The NMB group showed a non-significant reduction in 28-day mortality (34% vs. 42%, p=0.38), significantly more ventilator-free days (12.4 ± 5.1 vs. 9.1 ± 4.7, p=0.01), and lower barotrauma incidence (6% vs. 18%, p=0.04). **Conclusion:** Early NMB may improve ventilator-free days and reduce barotrauma in moderate-to-severe ARDS, though mortality benefit remains inconclusive.

## INTRODUCTION

ARDS is a life-threatening condition characterized by hypoxemia and decreased lung compliance. Lung-protective ventilation strategies have improved outcomes, but adjunctive therapies such as early neuromuscular blockade may further reduce ventilator-induced lung injury. This study evaluates the efficacy of early NMB compared to LPV alone.[1] Acute respiratory distress syndrome (ARDS) is a life-threatening condition characterized by refractory acute hypoxemia.[2] It is a major cause of morbidity and mortality in intensive care unit (ICU).[3,4] A number of interventions have been proposed in the past decade; however, few of them obtained strong recommendation.[5,6] Only lung-protective mechanical ventilation strategy has been proven beneficial for prognosis of these patients.[7] Neuromuscular blocking agents (NMBAs) may be a useful therapeutic strategy in patients with ARDS.[8] The ARDS et Curarisation Systematique (ACURASYS) trial conducted in 2010 found early administration of a 48-h infusion of NMBA was associated with a lower risk of death in patients with moderate-to-severe ARDS.[9] It is important to realize that patients in the control group in this study received deep sedation, and this is inconsistent with the current guidelines.[11,11]

**Objective:** To compare early NMB with LPV alone in patients with moderate-to-severe ARDS.

## MATERIALS AND METHODS

**Design:** Prospective, randomized, parallel-group trial
**Setting:** Tertiary care ICU, BLDE, Shri B M Patil Medical College & Research Centre (Deemed to be University), Vijayapura, Karnataka, India.
**Duration:** one year
**Participants:** Adults (18–75 years) with $PaO_2/FiO_2$ ≤150 mmHg on PEEP ≥5 cm $H_2O$
**Exclusion:** Pregnancy, neuromuscular disease, imminent death
**Intervention:**
- **Group A (NMB):** Cisatracurium infusion for 48 hours + LPV
- **Group B (Control):** LPV alone

**Ventilation Protocol:**
- Tidal volume: 6 mL/kg predicted body weight
- Plateau pressure ≤30 cm $H_2O$
- PEEP titrated per ARDSNet protocol

**Outcomes:**
- **Primary:** 28-day mortality
- **Secondary:** Ventilator-free days, ICU stay, barotrauma, SOFA score


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## RESULTS

**Table 1: Demographic information**

| Demographic Category | NMB Group (n=50) | LPV Group (n=50) | Total (n=100) |
|---|---|---|---|
| **Age (years)** | | | |
| 18–30 | 8 | 6 | 14 |
| 31–45 | 14 | 12 | 26 |
| 46–60 | 18 | 20 | 38 |
| >60 | 10 | 12 | 22 |
| **Mean ± SD** | 45.6 ± 13.2 | 47.1 ± 12.8 | 46.4 ± 13.0 |
| | | | |
| **Gender** | | | |
| Male | 32 | 30 | 62 |
| Female | 18 | 20 | 38 |

The majority of patients were between 31 and 60 years, accounting for 64% of the total cohort, specifically, 38% were aged 46–60 years, the largest subgroup. Younger adults (18–30 years) comprised 14%, while older adults (>60 years) made up 22%. The mean age was comparable between groups:

- NMB group: 45.6 ± 13.2 years
- LPV group: 47.1 ± 12.8 years
- This suggests balanced age distribution across intervention arms.

Gender Distribution

- Male patients predominated, representing 62% of the total sample.
  - NMB group: 32 males (64%)
  - LPV group: 30 males (60%)
- Female representation was slightly higher in the LPV group (40%) compared to the NMB group (36%).

**Table 2: Distribution according to outcome**

| Outcome | NMB Group (n=50) | LPV Group (n=50) | p-value |
|---|---|---|---|
| 28-day mortality (%) | 34 | 42 | 0.38 |
| Ventilator-free days | 12.4 ± 5.1 | 9.1 ± 4.7 | 0.01 |
| ICU length of stay (days) | 14.2 ± 6.3 | 16.1 ± 7.0 | 0.09 |
| Barotrauma incidence (%) | 6 | 18 | 0.04 |
| SOFA score (Day 3) | 7.8 ± 2.1 | 9.2 ± 2.5 | 0.02 |

This table provides description of the clinical outcome table comparing the two groups—early neuromuscular blockade (NMB) and lung-protective ventilation (LPV) alone—in patients with moderate-to-severe ARDS:

**Description of Clinical Outcomes**

**1. 28-Day Mortality: NMB group:** 34% and LPV group: 42%. Although the mortality rate was lower in the NMB group, the difference was not statistically significant (p = 0.38), suggesting a trend toward benefit but requiring larger sample sizes for confirmation.

**2. Ventilator-Free Days:** NMB group: 12.4 ± 5.1 days and LPV group: 9.1 ± 4.7 days. This difference was statistically significant (p = 0.01), indicating that patients receiving early NMB were liberated from mechanical ventilation earlier, reflecting better pulmonary recovery.

**3. ICU Length of Stay:** NMB group: 14.2 ± 6.3 days and LPV group: 16.1 ± 7.0 days. Although the NMB group had a shorter ICU stay, the difference was not statistically significant (p = 0.09), but it may still suggest a clinically meaningful reduction in resource utilization.

**4. Barotrauma Incidence:** NMB group: 6% and LPV group: 18%. This was a statistically significant reduction (*p = 0.04*) in the NMB group, supporting the hypothesis that muscle relaxation reduces ventilator-induced lung injury.

**5. SOFA Score on Day 3:** NMB group: 7.8 ± 2.1 and LPV group: 9.2 ± 2.5. The lower SOFA score in the NMB group (*p = 0.02*) suggests better early organ function, possibly due to reduced systemic inflammation and improved oxygenation.

Early neuromuscular blockade appears to confer benefits in ventilator-free days, barotrauma reduction, and early organ function, even though mortality and ICU stay did not reach statistical significance. These findings support the protective role of NMB in the acute phase of ARDS, aligning with prior evidence while highlighting the need for larger multicenter trials to confirm survival benefits.

## DISCUSSION

Early NMB was associated with improved ventilator-free days and reduced barotrauma, suggesting better lung protection. Although mortality differences were not statistically significant, the trend favors NMB. The reduction in SOFA scores indicates potential systemic benefit. Limitations include single-center design and modest sample size.

**Age Distribution**

Our study showed mean age ~46 years, with most patients (64%) between 31–60 years.

**LUNG SAFE Study,[11] (Global, n > 2800) observed that m**ean age: ~60 years and majority of patients were >50 years.


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**Indian Tertiary Care Study (Sheena Cherry et al,[12] 2020): observed that m**ean age: ~45 years and age distribution skewed toward 30–60 years, similar to your cohort.

**Interpretation:**

Your study aligns more closely with Indian ARDS cohorts in terms of age, reflecting a younger ICU population compared to global data. This may be due to differing epidemiology, healthcare access, or comorbidity profiles in India.

**Gender Distribution**

**Our study findings showed that** 62% male, 38% female.

**LUNG SAFE Study,[11] observed that** Male: ~60% and Female: ~40%

No significant gender-based outcome differences, though males had slightly higher severity scores.

**Indian Study (Sheena Cherry et al,[12]) showed that** Male: ~70% and Female: ~30%. Male predominance noted, consistent with higher ICU admission rates among men. Gender distribution is slightly more balanced than typical Indian cohorts but still shows male predominance, consistent with global ARDS epidemiology. This may reflect higher exposure to risk factors (e.g., smoking, occupational hazards) among men.

**Table 3: Comparative analysis of outcome with other study findings**

| Outcome | Our Study (India, n=100) | ACURASYS Trial[13] (France, n=340) | ROSE Trial[14] (USA, n=1006) |
|---|---|---|---|
| **28-Day Mortality** | 34% (NMB) vs. 42% (LPV), *p*=0.38 | 31.6% (NMB) vs. 40.7% (Placebo), *p*=0.04 | 42.5% (NMB) vs. 42.8% (Usual care), *p*=0.93 |
| **Ventilator-Free Days** | 12.4 vs. 9.1, *p*=0.01 | Not reported directly; improved oxygenation noted | No significant difference |
| **ICU Length of Stay** | 14.2 vs. 16.1 days, *p*=0.09 | No significant difference | No significant difference |
| **Barotrauma Incidence** | 6% vs. 18%, *p*=0.04 | Lower in NMB group (not primary endpoint) | No significant difference |
| **SOFA Score (Day 3)** | 7.8 vs. 9.2, *p*=0.02 | Lower in NMB group at 48h (*p*=0.01) | No significant difference |
| **Sedation Strategy** | Not specified (likely moderate) | Deep sedation in both groups | Lighter sedation in control group |

**Interpretation**

- **Mortality**: Your study shows a non-significant trend toward reduced mortality with NMB, echoing ACURASYS but contrasting with ROSE, which found no benefit. The discrepancy may stem from sedation practices—ROSE used lighter sedation, potentially reducing the need for NMB.
- **Ventilator-Free Days**: Your significant improvement mirrors the physiological rationale of NMB—better synchrony and reduced lung injury. ROSE did not replicate this, possibly due to protocol differences.
- **Barotrauma and SOFA Score**: Both our study and ACURASYS show reductions, suggesting early NMB may mitigate systemic inflammation and mechanical stress. ROSE did not find these benefits, again highlighting the role of sedation depth and patient selection.

"Our findings align with the ACURASYS trial, which demonstrated improved oxygenation and reduced mortality with early NMB under deep sedation. In contrast, the ROSE trial, employing lighter sedation, found no mortality or ventilator benefit. The discrepancy underscores the importance of sedation strategy and patient selection in interpreting NMB efficacy. The reduction in barotrauma and SOFA scores in our cohort supports the hypothesis that early muscle relaxation may attenuate ventilator-induced lung injury and systemic inflammation.

## CONCLUSION

In patients with moderate-to-severe ARDS, early neuromuscular blockade may enhance lung protection and improve short-term outcomes. Larger multicenter trials are warranted to confirm mortality benefits.

**Conflict of interest:** Nil

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