ISCCM
INDIAN SOCIETY OF CRITICAL CARE MEDICINE

CRITICAL CARE UPDATE 2026

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8th Edition

JAYPEE

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2.3 CHAPTER

Prone Positioning in Venovenous Extracorporeal Membrane Oxygenation

Dhruva Chaudhry, Monalisa Mishra, Abu Nadeem

INTRODUCTION

Acute respiratory distress syndrome (ARDS) remains a major contributor to morbidity and mortality among critically ill patients. Even with advancements in lung-protective ventilation strategies, outcomes in severe ARDS continue to be poor. Venovenous extracorporeal membrane oxygenation (VV-ECMO) provides extracorporeal support for gas exchange in patients with persistent hypoxemia or hypercapnia, enabling the lungs to rest and recover. Prone positioning (PP) has independently demonstrated benefits in oxygenation and survival for patients with moderate-to-severe ARDS, particularly when implemented for prolonged durations of 16 hours or more each day.[1]

Over the past decade—especially during the COVID-19 pandemic, when the incidence of ECMO use increased substantially—the concurrent use of PP during VV-ECMO has received growing interest. This combined approach aims to enhance ventilation–perfusion (V/Q) matching and support lung healing, although current evidence regarding its impact on clinical outcomes remains inconclusive.

This chapter explores the underlying physiological basis, current clinical data, safety profile, procedural aspects, and practice recommendations for employing PP in patients undergoing VV-ECMO support.

PATHOPHYSIOLOGICAL RATIONALE

Acute Respiratory Distress Syndrome and Ventilator-induced Lung Injury

Acute respiratory distress syndrome is characterized by diffuse alveolar damage, resulting in pulmonary edema, a reduction in functional lung volume (referred to as the "baby lung"), collapse of dependent lung regions, and an uneven distribution of ventilation. Although mechanical ventilation is vital for maintaining gas exchange, it can inadvertently worsen lung injury through excessive pressure and volume stress—collectively known as ventilator-induced lung injury (VILI).[2]

Impact of Prone Positioning

Placing patients in the prone position helps redistribute transpulmonary pressures, reduces compression of the dorsal lung by the heart, and promotes recruitment of the posterior lung segments.[3] This posture enhances homogeneity of ventilation, improves drainage of secretions, limits dorsal atelectasis, and enhances arterial oxygenation by decreasing intrapulmonary shunting.[4]

Impact of VV-ECMO

Venovenous ECMO provides extracorporeal oxygenation and carbon dioxide removal, allowing the use of ultraprotective ventilatory settings with lower tidal volumes, airway pressures, and inspired oxygen concentrations. Nevertheless, despite ECMO support, lung collapse and ventilation inhomogeneity may persist, maintaining regional overdistension and cyclic stress.[5]

Combined Benefits of PP and VV-ECMO

Integrating PP with VV-ECMO theoretically counteracts residual atelectasis during extracorporeal support, improving gas exchange, compliance, and regional ventilation while mitigating further ventilator-induced injury. ECMO maintains adequate systemic oxygenation during prone sessions, whereas proning may accelerate lung recruitment and recovery, potentially facilitating earlier ECMO weaning[6] **(Table 1)**.

EVIDENCE SUMMARY

Observational and Retrospective Studies

Early single-center studies established the feasibility and physiologic benefit.

- *Giani et al. (2015)* studied 17 ARDS patients on VV-ECMO undergoing 27 sessions of 24-hour PP.

TABLE 1: Physiological effects of proning during VV-ECMO.

Parameter	*Effect*	*Clinical significance*	*Key evidence*
PaO_2/FiO_2	↑ 40–70 mm Hg	Improves refractory hypoxemia	Giani, Poon
Respiratory compliance	↑ 5–15 mL/cmH_2O	Suggests alveolar recruitment	Giani, Lucchini
$PaCO_2$	↓ 5–10 mm Hg	Enhanced CO_2 clearance	Poon
Driving pressure	↓	Less VILI	Poon
ECMO flow	Stable	Safe maneuver	Multiple studies
Hemodynamics	Mostly stable	Minimal cardiovascular compromise	Lucchini

PaO_2/FiO_2 improved from 111 ± 40 to 173 ± 72 mm Hg and compliance from 18 ± 7 to 32 ± 12 mL/cmH_2O. Hemodynamics remained stable, and no major complications occurred.[7]

- *Rilinger et al. (2020)* retrospectively analyzed 158 ECMO patients (38 proned). Early PP (<17 hours after ECMO initiation) was associated with higher survival (81.8% vs. 33.3%), though overall mortality did not differ significantly.[8]
- *Lucchini et al. (2020)* in COVID-19 ARDS found that PP during ECMO improved PaO_2/FiO_2 and compliance without major ECMO flow disturbances, confirming safety in this subset.[9]
- *BMC Pulmonary Medicine cohort (2022)* showed improved oxygenation but no difference in ICU or hospital survival between PP + ECMO and ECMO-alone groups.[10]
- *Bleeding risk:* In a cohort of 136 ECMO patients, PP did not increase bleeding compared with supine (61% vs. 53%; $p = 0.29$).[11]

Systematic Reviews and Meta-Analyses

- *Poon et al. (2021)* analyzed 12 studies (640 patients). PP during VV-ECMO improved oxygenation ($\Delta PaO_2/FiO_2 \approx +45$ mm Hg) and compliance, reduced $PaCO_2$, and did not raise complication rates. Survival at hospital discharge was 57% (95% CI 42–71).[12]
- *Guervilly et al. (2023)* found that PP + ECMO improved early (30-day) survival and oxygenation but not 60- or 90-day mortality.[13]

Randomized Trial: PRONECMO (2023)

The *PRONECMO trial* randomized 170 patients with severe ARDS on VV-ECMO <48 hours to receive ≥4 sessions of 16-hour PP versus continued supine management. The primary outcome—time to successful ECMO weaning—showed no significant difference between groups (HR 1.02, 95% CI 0.77–1.35). Ninety-day mortality (39% vs. 45%) and adverse event rates were also similar **(Fig. 1)**.[14]

Interpretation: PP during ECMO is safe and physiologically beneficial, but does not yet demonstrate a mortality advantage in randomized evidence.

The clinical evidence regarding PP during ECMO is mixed **(Table 2)**, showing benefits like improved oxygenation and compliance in some studies, but with no consistent survival advantage across all trials.

SAFETY AND COMPLICATIONS

Cannula-related Complications

Repositioning a patient supported on VV-ECMO presents potential hazards, particularly the risk of cannula displacement, kinking, or tension on the circuit lines. These events could compromise ECMO flow or lead to catastrophic bleeding if a cannula becomes dislodged. Nonetheless, in high-volume centers with well-trained teams and standardized proning protocols, such complications are exceedingly uncommon, with reported incidences of dislodgement below 1%.[7,10] Close coordination between nursing, perfusion, and medical teams, along with meticulous pre- and post-turn checks, is our key preventive measure.

Hemodynamic Instability

Prone positioning may transiently influence cardiovascular dynamics by altering venous return, pulmonary vascular resistance, and right ventricular afterload. Despite these theoretical risks, most clinical studies report minimal hemodynamic disturbance, with stable mean arterial pressures and cardiac output throughout proning sessions. Occasional transient increases in vasopressor

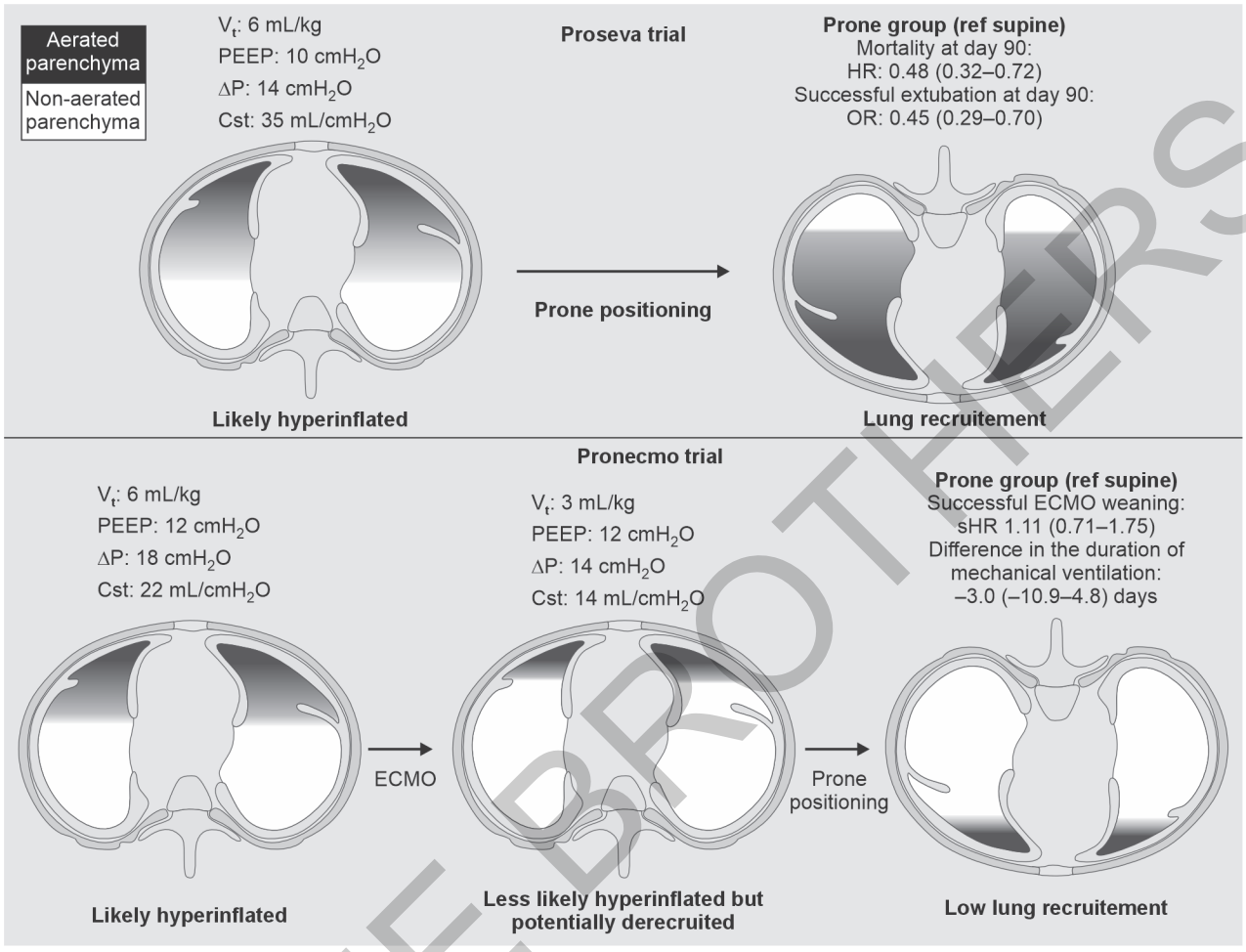

Fig. 1: This illustration contrasts how PP produces substantial lung recruitment and survival benefit in conventionally ventilated ARDS (PROSEVA) but offers minimal additional recruitment and no major clinical advantage during ultraprotective ventilation on ECMO (PRONECMO).[15]

TABLE 2: Summary of key clinical studies on the use of prone positioning (PP) in patients receiving ECMO.

Study	*Design*	*Patients*	*Key findings*
Giani (2015)	Prospective	17	↑ PF ratio, ↑ compliance, safe
Rilinger (2020)	Retrospective	158	Early PP ↑ survival, but overall mortality is similar
Lucchini (2020)	COVID ARDS	30+	Improved oxygenation, stable flow
Zhang (2022)	Cohort	136	Improved oxygenation; no survival benefit
Poon (2021)	Meta-analysis	640	↑ Oxygenation/compliance; no ↑ complications
PRONECMO (2023)	RCT	170	No difference in ECMO weaning/mortality

requirements may occur, particularly during the turning maneuver or in patients with marginal preload reserve, but these are generally mild and do not necessitate aborting the session.[9] Continuous monitoring and gradual repositioning help ensure stability.

Bleeding and Anticoagulation Considerations

Because patients on VV-ECMO require systemic anticoagulation to prevent circuit thrombosis, the risk of bleeding is always a concern. However, comparative studies have shown that the incidence of major bleeding,

including airway or cannula-site hemorrhage, does not rise during prone sessions.[11] With careful monitoring of anticoagulation targets and avoidance of unnecessary line manipulation, proning can be performed safely without increasing transfusion requirements.

Pressure Injuries and Skin Integrity

Prolonged prone sessions—often lasting 16–24 hours—predispose patients to pressure-related injuries, especially on the forehead, cheeks, chin, and anterior thorax. Reported rates of pressure ulcers range from 10 to 20% and most are minor (grades I and II).[9] These injuries are largely preventable through the use of protective padding, frequent repositioning of the head and limbs, and regular skin inspection by nursing staff. Employing specialized proning beds or foam supports can further minimize these complications.

Oxygenator Thrombosis and ECMO Flow Alterations

During PP, rare instances of transient ECMO flow reduction or oxygenator clot formation have been documented, occurring in approximately 3% of cases.[7] These changes are typically attributed to mechanical kinking, increased intrathoracic pressure, or transient malalignment of the cannula. Prompt identification, minor position adjustments, and vigilant circuit monitoring generally restore normal flow without lasting impact. Routine observation of circuit pressures and visual assessment of tubing and cannulas during patient repositioning are crucial for preventing complications.

INDICATIONS AND TIMING

Indications

Prone positioning during VV-ECMO should be considered in patients who continue to exhibit *severe hypoxemia* despite optimal ventilator settings and adequate ECMO support. It is particularly useful when *lung compliance remains poor* or *driving pressures exceed 15 cmH_2O*, indicating ongoing alveolar collapse and regional overdistension. Patients who demonstrate *difficulty in weaning from ECMO*, especially after prolonged runs (≥7 days), may also benefit from proning to recruit dorsal lung regions and enhance lung mechanics. Additionally, *radiological findings* such as posterior or dorsal consolidations on chest imaging suggest the presence of *recruitable lung tissue*, supporting the rationale for implementing PP.[16]

Timing

Current evidence favors *early initiation* of PP—ideally within the first *24 hours after ECMO commencement*—as early sessions appear to yield greater improvements in oxygenation and may facilitate earlier lung recovery.[8] Nevertheless, *late proning* (after 7 days of ECMO) can still provide transient improvements in gas exchange, although its effect on survival or ECMO duration appears limited. Thus, timing should be individualized based on patient stability, lung recruitability, and overall trajectory.

Session Duration and Frequency

Typical sessions last *16–24 hours*, repeated daily or every other day depending on response.[7,14] Longer sessions appear to yield greater and more sustained improvements.

PROCEDURAL CONSIDERATIONS

Preparation

1. Confirm that all ECMO cannulas are securely anchored and that sufficient circuit slack is available to prevent traction or kinking during repositioning.
2. Provide adequate sedation, with or without neuromuscular blockade, to ensure patient immobility and safety during proning.
3. Adjust ventilator settings to an ultraprotective strategy—tidal volume ≤4 mL/kg predicted body weight, plateau pressure <25 cmH_2O, and moderate PEEP levels.
4. Maintain ECMO blood flow between 4 and 6 L/min and titrate FiO_2 to keep SpO_2 above 88%.
5. Ensure the availability of a well-trained multidisciplinary team, typically five or more members, including nurses, respiratory therapists, and perfusionists.

Proning Maneuver

The rotation should be performed in a systematic, team-coordinated manner using draw sheets or automated proning beds to minimize risks. The patient's head is turned laterally with proper support, and all ECMO cannulas are continuously observed to prevent displacement or obstruction throughout the procedure **(Table 3)**.

TABLE 3: Procedural checklist for proning in VV-ECMO.

Step	*Key actions*
Before proning	Secure cannulas; ensure circuit slack; sedation ± NMB; optimize ventilator; prepare team; check hemodynamics
During maneuver	Team-coordinated turn; continuous cannula and circuit visualization; maintain line patency
During prone period	Lung-protective ventilation; monitor ECMO flow/pressures; pressure point checks; ABGs at intervals
After supination	Reassess mechanics and oxygenation; check cannula position; document responses

Monitoring

- Continuous monitoring of oxygen saturation, hemodynamic parameters, and ECMO flow and pressures is essential.
- Arterial blood gases should be assessed before, during, and after prone sessions to evaluate response.
- Skin integrity, especially at pressure points, must be checked every 2–3 hours.
- If there is a >20% drop in PaO_2 or a >10% fall in ECMO flow, the patient should be promptly returned to the supine position.

Contraindications

- Severe or unstable hemodynamic conditions.
- Recent median sternotomy, unstable spinal injury, or elevated intracranial pressure
- Abdominal compartment syndrome or open abdominal wounds
- Morbid obesity where safe repositioning cannot be achieved.[17]

OUTCOMES

Oxygenation and Respiratory Mechanics

The majority of available studies consistently report marked, short-term enhancement in oxygenation and respiratory compliance following PP in patients supported with VV-ECMO.[7-10,12] These physiological improvements typically occur within hours of proning but may be temporary, often waning once the patient is repositioned to the supine posture. The benefits are attributed to improved alveolar recruitment, more homogeneous ventilation, and reduced dorsal atelectasis.

ECMO Duration and Weaning

The influence of PP on the total duration of ECMO support and weaning success remains uncertain. While some centers have observed expedited ECMO liberation when proning is introduced early—within the initial phase of support[8]—other investigations, such as the PRONECMO study, have reported no significant difference in ECMO duration or decannulation rates.[14] These discrepancies likely reflect variations in patient selection, timing of intervention, and local practice protocols.

Survival

Evidence from meta-analyses suggests that PP during ECMO may confer a modest short-term survival benefit, yet this does not consistently translate into improved long-term outcomes.[12,13] The survival effect appears to be more pronounced in specific subgroups, notably patients who receive early proning, exhibit high potential for alveolar recruitment, or have non-COVID-related ARDS. This highlights the importance of individualized assessment rather than universal application of the technique.

Intensive Care Unit Length of Stay

Patients treated with combined PP and VV-ECMO often experience prolonged ECMO runs and extended ICU stays. This observation likely reflects a selection bias—these patients typically have more severe disease and slower recovery trajectories—rather than a detrimental effect of the intervention itself.[12] Nevertheless, careful patient selection and standardized weaning protocols may mitigate prolonged ICU occupancy.

IMPLEMENTATION IN CLINICAL PRACTICE

Institutional Protocol Example

Based on recommendations from ELSO and national critical care guidelines,[16,17] a structured approach for PP during VV-ECMO **(Table 4)** can be outlined as follows:

- *Eligibility:* Proning is considered for patients with *refractory hypoxemia* on VV-ECMO (PaO_2/FiO_2 <80) and evidence of *recruitable lung tissue* on imaging studies.
- *Preprone checklist:*
  - Confirm *secure fixation of all ECMO cannulas*.
  - Organize *lines and tubing* to prevent traction or kinking.

TABLE 4: Complications and preventive measures.

Complication	*Incidence*	*Mechanism*	*Prevention*
Cannula displacement	<1%	Traction/kinking during turn	Secure fixation, trained team
Hemodynamic instability	Mild/transient	↓ Preload or ↑ PVR	Gradual turning, adequate fluids/vasopressors
Bleeding	No significant increase	Anticoagulation + pressure points	Monitor ACT/APTT, pad bony areas
Pressure ulcers	10–20%	Prolonged pressure	Foam dressings, position changes
ECMO flow reduction	~3% transient	Cannula malalignment/kink	Real-time circuit checks

  - Ensure *adequate sedation*, neuromuscular blockade if needed, and hemodynamic stability.
- *During prone positioning:*
  - Continue *lung-protective ventilator strategies*.
  - Adjust ECMO sweep gas and FiO_2 according to oxygenation and CO_2 clearance targets.
  - Conduct *regular checks of limbs, face, and ECMO circuit* to prevent pressure injuries or cannula complications.
- *Postprone management:*
  - Reassess *gas exchange, oxygenation, and lung compliance*.
  - Record any *adverse events or complications*.
  - Plan and repeat sessions as required until there is *sustained improvement* in oxygenation and mechanics.

Staffing and Safety

- The proning team typically includes an *intensivist, ECMO specialist, bedside nurse, respiratory therapist, and physiotherapist*.
- Establish *clear communication protocols*, including predefined commands and contingency plans for emergent supination if needed.
- Maintain meticulous *documentation* of timing, physiological responses, and any complications for quality assurance and audit purposes.

LIMITATIONS OF CURRENT EVIDENCE

- Most studies are *retrospective*, carrying inherent risks of selection and reporting bias.
- *Confounding by severity* exists, as patients with more severe ARDS are more likely to receive PP, potentially skewing outcomes.
- There is considerable *heterogeneity in protocols*, including variations in session duration, timing of initiation, and ventilator settings across centers.
- Many datasets are *COVID-19–dominant*, which may limit applicability to non-COVID ARDS populations.
- *Outcome measures* differ across studies, with some reporting 28-day mortality and others 90-day or ICU mortality, making direct comparisons challenging.
- There is a *lack of long-term follow-up*, particularly regarding pulmonary function, exercise tolerance, and quality of life after ECMO and proning.

Practical Recommendations

- *Early implementation:* Initiate PP promptly in VV-ECMO patients whose oxygenation remains inadequate despite optimized ECMO flows and PEEP settings.
- *Prolonged sessions:* Maintain proning for extended durations (16–24 hours) to achieve maximal alveolar recruitment and improved gas exchange.
- *Team preparedness:* Ensure that all members of the multidisciplinary team are adequately trained, and use standardized checklists to enhance safety and coordination.
- *Complication surveillance:* Closely monitor for potential adverse events, particularly *pressure ulcers* and ECMO circuit or cannula issues.
- *Objective evaluation:* Record physiological responses—PaO_2/FiO_2 ratio, compliance, and other relevant parameters—after each session to guide further proning decisions.
- *Individualized approach:* Do not apply PP universally to all ECMO patients; tailor use based on *lung morphology, recruit ability, and hemodynamic stability*.
- *Lung-protective strategy:* Continue ultraprotective ventilatory settings regardless of patient position
- *Research directions:* Future studies should investigate *cost-effectiveness* and *long-term outcomes*, including pulmonary function, exercise capacity, and quality of life.

CONCLUSION

Prone positioning during VV-ECMO merges two complementary strategies for severe ARDS management. Physiological and observational data consistently show improved oxygenation and compliance without major safety concerns. The largest randomized trial confirms feasibility and safety, but no clear mortality benefit. Prone positioning should therefore be viewed as an *adjunct*—not a routine intervention—for selected patients with refractory hypoxemia, recruitable lungs, and stable hemodynamics, within experienced centers following standardized protocols. Continued investigation into timing, patient selection, and long-term outcomes will clarify its definitive role in the modern ECMO era.

TAKE HOME MESSAGE

1. *PP during VV-ECMO is safe and feasible* in experienced centers, with minimal cannula or circuit complications.
2. It provides *consistent short-term physiological benefits*—better oxygenation, improved compliance, and reduced driving pressures.
3. *Clinical outcome improvements remain uncertain*; the PRONECMO trial showed no advantage in ECMO weaning or mortality.
4. *Early and prolonged sessions (16–24 hours)* offer the greatest benefit, especially in patients with recruitable dorsal lung regions.
5. PP should be used *selectively as an adjunct*, not routinely, based on lung morphology, hemodynamic, and center expertise.

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ISBN 978-93-7545-461-8