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CLINICAL OUTCOMES OF PRONE POSITIONING IN PATIENTS WITH ACUTE RESPIRATORY DISTRESS SYNDROME: A SYSTEMATIC REVIEW OF RANDOMIZED AND OBSERVATIONAL STUDIES

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Abstract

Background: Prone positioning is a recommended intervention for patients with moderate to severe acute respiratory distress syndrome (ARDS). Its physiologic benefits include improved oxygenation and lung mechanics. Its impact on mortality, especially in patients receiving extracorporeal membrane oxygenation (ECMO), is variable. We aimed to systematically review the clinical outcomes of prone positioning in adult ARDS patients, including those supported with mechanical ventilation or veno-venous ECMO. **Methods:** This review according to PRISMA 2020 guidelines. A search was conducted in PubMed, Scopus, Web of

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Science, and Google Scholar for English-language studies published between 2010 and 2025. Randomized controlled trials, cohort studies, and case series were included. We include studies in prone positioning outcomes in adult ARDS patients receiving mechanical ventilation or ECMO. Data were extracted on mortality, oxygenation indices (PaO_2/FiO_2), ventilation duration, ECMO weaning, and complications. **Results:** Eleven studies were included (2 randomized controlled trials, 6 cohort studies, 2 case series, and 1 propensity-matched study). Most studies reported improved oxygenation after prone positioning. Several studies identified early PaO_2/FiO_2 improvement as a survival predictor. Mortality was lower in early and prolonged prone sessions, mainly when used in conjunction with lung-protective ventilation. In ECMO patients, prone positioning was feasible, improved oxygenation, and was not associated with increased complications. Not all studies show statistically significant survival benefits. **Conclusion:** Prone positioning improves oxygenation and reduce mortality in moderate to severe ARDS, mainly when applied early and for ≥12 hours per session. It is safe in patients receiving ECMO, with oxygenation response serving as a prognostic marker.

Keywords: Prone Positioning, ARDS, Acute Respiratory Distress Syndrome, ECMO, Mechanical Ventilation, Oxygenation, Mortality, VV-ECMO, Pao_2/Fio_2, Ventilation Outcomes.

INTRODUCTION

Acute respiratory distress syndrome (ARDS) is bilateral pulmonary infiltrates and severe hypoxemia not due to cardiac failure or fluid overload, and associated with high mortality rates of 35–45% in modern cohorts (1,2).

Prone positioning (originally proposed in the 1970s) gained interest in ARDS management due to its physiological benefits, improved dorsal lung recruitment, more uniform ventilation, and attenuated ventilator-induced lung injury (1,2).

The PROSEVA randomized controlled trial showed that early initiation of prone positioning for ≥16 h/day reduced 28 and 90 day mortality in severe ARDS compared to supine care (3).

Park et al. (2015) show that prone positioning coupled with lung-protective ventilation and prolonged sessions (>12 h/day) improved survival rates. Munshi et al. (2017) concluded that prone positioning offers a mortality benefit in moderate to severe ARDS (PaO_2/FiO_2 < 150 mmHg), thereby supporting inclusion in practice guidelines (1,2).

During the COVID-19 pandemic, interest increase in applying prone positioning in patients supported with venovenous extracorporeal membrane oxygenation (VV-ECMO). A multicenter cohort study (240 adults in six Italian centers) show that prone positioning during ECMO improved oxygenation and associated with lower hospital mortality (OR 0.50; 95% CI 0.29–0.87), with minor complications reported (4).

Another pooled individual patient data analysis of five European cohort studies found ICU mortality rates were lower in the prone ECMO group (39.6%) than supine (48.0%), without reaching statistical significance (p = .072) (5).

A Frontiers in Medicine prospective analysis in COVID-19 ARDS patients on ECMO showed that prone positioning increased PaO_2/FiO_2 by 14 ± 21% and compliance by 8 ± 15% during 16-h sessions, with respiratory mechanics benefits post repositioning and no major side effects (6).

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A newer meta-analyses found that prone positioning during VV-ECMO reduces 28 days and hospital mortality (7).

Variability exists in clinical protocols regarding timing, session duration, and patient selection mainly in trauma or postoperative populations at risk for complications (8).

Our systematic review synthesizes evidence from adult ARDS patients receiving mechanical ventilation or VV-ECMO to elucidate prone positioning's impact on mortality, oxygenation, ventilator/ECMO duration, and safety.

METHODS

This systematic review was conducted according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines (Fig 1). We aimed to evaluate the clinical outcomes of prone positioning in adult patients with acute ARDS receiving mechanical ventilation or extracorporeal membrane oxygenation (ECMO).

We include randomized controlled trials (RCTs), retrospective and prospective cohort studies, and case series. Included studies were published in English between 2010 and 2025.

We include studies with adult patients (aged ≥18 years) diagnosed with ARDS using the Berlin definition, and underwent at least one session of prone positioning. Interventions of interest included prone positioning used in mechanically ventilated patients, with or without concurrent ECMO support.

Studies that reported relevant clinical outcomes (mortality, oxygenation indices [PaO_2/FiO_2], duration of ventilation, ECMO weaning, or procedure-related complications) were included. We exclude studies with pediatric populations, conference abstracts without full text, narrative reviews, and case reports.

A literature search was conducted in electronic databases (PubMed/MEDLINE, Scopus, Web of Science, and Google Scholar). The search strategy included keywords (prone positioning, prone ventilation, ARDS, acute respiratory distress syndrome, mechanical ventilation, and ECMO). The final search was performed in March 2025. The reference lists of selected articles were screened manually to identify additional relevant studies.

Study selection was performed by two reviewers who screened the titles and abstracts. Full-text articles were retrieved for eligible studies. Discrepancies between reviewers were resolved through discussion. A standardized data extraction form was used to collect data on study characteristics, sample size, inclusion criteria, patient demographics, intervention details, clinical outcomes, and adverse events.

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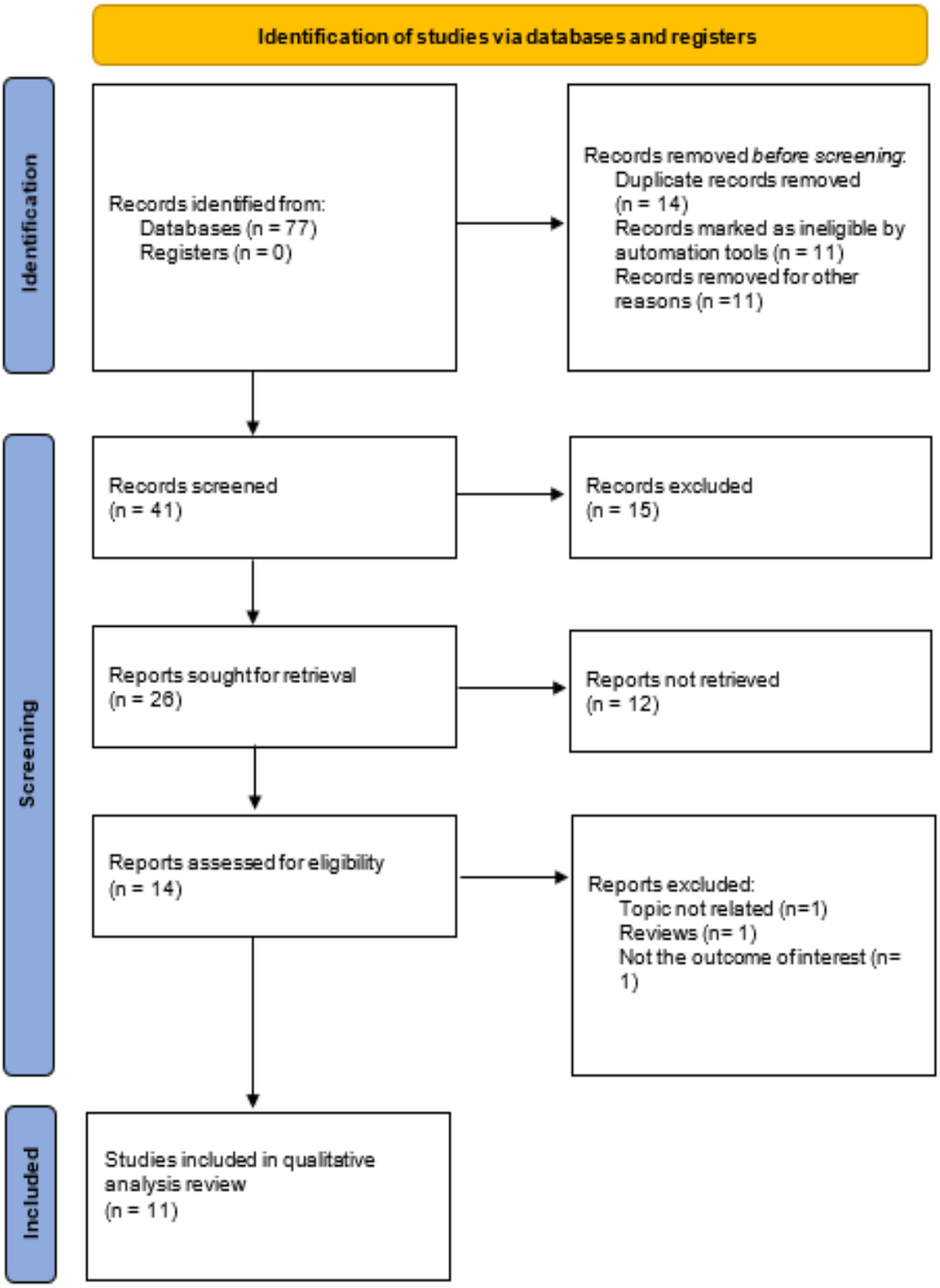

Fig 1: PRISMA consort chart

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RESULTS

Study Selection

A total of 11 studies published between 2010 and 2025 were included in this systematic review. These comprised two randomized controlled trials (RCTs), six retrospective cohort and observational studies, two case series, and one propensity-matched cohort study. The studies examined the clinical impact of prone positioning in patients with ARDS, including mechanically ventilated and ECMO-supported patients.

Study Characteristics

The included studies differ in design, population size, and ARDS severity. Sample sizes ranged from 9 to 466 patients. Most patients had moderate to severe ARDS, and some studies involved patients receiving veno-venous extracorporeal membrane oxygenation (VV-ECMO).

Two studies evaluated early prone positioning in combination with ECMO support. Demographic profiles were comparable in studies, with mean ages ranging from 42 to 64 years and a predominance of male patients. The inclusion criteria targeted patients with $PaO_2/FiO_2 \leq 150$ mmHg, who need mechanical ventilation or ECMO (Table 1).

Clinical Outcomes

Regarding mortality reduction, Guérin et al. (3) find a significant reduction in both 28-day and 90-day mortality with prone positioning (16% vs. 32.8% and 23.6% vs. 41%, respectively). Rilinger et al. (2020) and Liang et al. (2024) reported lower ICU or 28-day mortality in responders to prone positioning (9,10). In Chen et al. (2022) and Giani et al. (2020), mortality is better in prone positioning during ECMO, and not always reach significance level (11,12).

All studies reported improved oxygenation (PaO_2/FiO_2 ratios) after prone positioning. Lee et al. (2020) and Kwangha Lee et al. (2010) found that early oxygenation improvement was predictive of survival (13,14).

Yan et al. (2025) found a significant oxygenation improvements and identified late intubation as a predictor of poor outcome (15). Schmidt et al. (2023) found no significant difference in ECMO weaning or 90-day mortality (16). Giani et al. (2020) and Guervilly et al. (2014) show improved oxygenation of prone positioning during ECMO, with low complication rates (12,17).

In all studies, prone positioning was found to be safe, including when applied during ECMO. Reported complications (pressure ulcers, catheter dislodgements) were infrequent and manageable. None of the included studies reported significant differences in adverse events between prone and supine groups.

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Table 1: Summary of studies on prone positioning in ARDS patients

Citation	Study Design	Sample Size	Inclusion Criteria	Study Aim
Guérin et al., 2013 (3)	Randomized Controlled Trial	466 patients	Adults with severe ARDS (PaO2/FiO2 < 150 mmHg, FiO2 ≥ 0.6, PEEP ≥ 5 cmH2O)	To assess if early prolonged prone positioning reduces mortality in severe ARDS
Schmidt et al., 2023 (16)	Randomized Controlled Trial	170 patients	Severe ARDS patients on VV-ECMO < 48 hours	To determine if prone positioning reduces time to ECMO weaning compared to supine
Giani et al., 2020 (12)	Multicenter retrospective cohort, propensity-matched	240 patients	ARDS patients supported with VV-ECMO	To assess feasibility, safety, and outcomes of prone positioning during ECMO
Chen et al., 2022 (11)	Retrospective cohort	91 patients	ARDS per Berlin definition, on VV-ECMO	To evaluate safety and efficacy of prone position during VV-ECMO
Rilinger et al., 2020 (9)	Retrospective cohort	158 patients	Severe ARDS patients on VV-ECMO	To determine the effect of prone positioning on ECMO weaning and hospital survival
Liang et al., 2024 (10)	Retrospective observational	104 patients	Invasively ventilated adults with ARDS receiving ≥ 3 PPV sessions ≥ 6h each	To evaluate if oxygenation improvement after PPV predicts survival
Lee et al., 2020 (14)	Retrospective observational	116 patients	Moderate-to-severe ARDS receiving prone positioning	To assess if oxygenation response to prone positioning predicts survival
Kwangha Lee et al., 2010 (13)	Retrospective observational	96 patients	Severe ARDS (PaO2/FiO2 ≤ 150 mmHg) in ICU	To evaluate the significance of early oxygenation improvement with prolonged prone positioning
Guervilly et al., 2014 (17)	Retrospective cohort	15 patients	Severe ARDS patients on VV-ECMO with hypoxemia or failure to wean	To evaluate the effect and safety of prone positioning during ECMO
Kredel et al., 2014 (18)	Case series	9 patients	Severe ARDS patients treated with VV-ECMO and positioning therapy	To describe feasibility and complications of combining positioning therapy with ECMO
Yan et al., 2025 (15)	Retrospective observational cohort	234 patients	ARDS patients receiving ≥1 prone positioning session between 2015–2023	To evaluate survival benefit and prognostic predictors after prone positioning in ARDS

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Table 2: Findings Summary of Prone Positioning in ARDS Patients

Citation	Demographic Characteristics	Main Findings	Outcomes
Guérin et al., 2013 (3)	Mean age =60 years; predominantly male; severe ARDS (P/F < 150)	Early prolonged prone positioning significantly reduced 28- and 90-day mortality	28-day mortality: 16% (prone) vs. 32.8% (supine); 90-day mortality: 23.6% vs. 41%
Schmidt et al., 2023 (16)	Mean age =52 years; most on VV-ECMO for <48h	No significant difference in ECMO weaning or 90-day survival between groups	90-day survival: 51% (prone) vs. 48% (supine); similar complications
Giani et al., 2020 (12)	Mean age = 54; ECMO patients; matched by propensity score	Prone during ECMO was feasible and associated with improved oxygenation	Better ECMO duration and oxygenation in prone group
Chen et al., 2022 (11)	Median age =51; all on VV-ECMO; severe ARDS	Prone position improved PaO2/FiO2 and compliance	Significant oxygenation improvement in prone group; safe with minimal complications
Rilinger et al., 2020 (9)	Median age =56; ECMO support for severe ARDS	Prone associated with higher survival and ECMO weaning rates	ICU mortality lower in prone group; ECMO weaning more successful
Liang et al., 2024 (10)	Median age 64; mostly male; ARDS on mechanical ventilation	Responders to PPV had better survival; early PaO2/FiO2 changes predictive	28-day survival higher in oxygenation responders ($p < 0.001$)
Lee et al., 2020 (14)	Mean age =63; mixed ARDS severity	Responders to prone had significantly lower mortality	Mortality: 20.5% (responders) vs 50% (non-responders)
Kwangha Lee et al., 2010 (13)	Mean age =57; ICU patients with severe ARDS	Early oxygenation improvement predicted survival	Improved PaO2/FiO2 associated with ICU survival
Guervilly et al., 2014 (17)	Mean age =42; 15 ECMO patients	Prone improved oxygenation without major complications	Mean PaO2/FiO2 improved from 66 to 120 mmHg
Kredel et al., 2014 (18)	Mean age =45; 9 patients with ARDS on ECMO	Prone and lateral positioning feasible and safe on ECMO	Improved ventilation parameters; no major device dislodgement
Yan et al., 2025 (15)	Mean age =60; 234 ARDS patients prone positioned (2015–2023)	Improved survival and PF ratio post prone; late intubation predicted poor outcome	28-day mortality: 34%; PF improvement predicted better prognosis

DISCUSSION

Our systematic review examined clinical outcomes associated with prone positioning in patients with ARDS, including those supported with veno-venous extracorporeal membrane oxygenation (VV-ECMO). In 11 studies of different designs (randomized controlled trials, retrospective cohorts, and observational analyses) our findings align closely with previously published meta-analyses regarding the impact of prone positioning

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on oxygenation and mortality. The PROSEVA trial, included in our review (3) and earlier meta-analyses by Munshi et al. (1), indicate a reduction in mortality with early and prolonged prone positioning. Our review corroborated these results; prone positioning, particularly when initiated early and maintained for ≥12 hours, was associated with improved PaO_2/FiO_2 ratios and lower 28- or 90-day mortality.

Studies by Liang et al. (10) and Lee et al. (14) showed that early oxygenation improvements strongly predicted survival, affirming the prognostic utility of early response to prone therapy. The meta-analysis by Park et al. (2) show that longer durations (>12 hours) of prone positioning, combined with lung-protective ventilation, reduced mortality (RR 0.73, 95% CI 0.62–0.86). These findings were similar to outcomes from our included studies Rilinger et al. and Giani et al. who showed increased weaning success and survival in prone ECMO patients. These underscore the relevance of implementing prolonged prone sessions as part of routine ARDS care protocols (9,12).

Phoophiboon et al. (8) extended this discussion into trauma and surgical ARDS populations, showing improved PF ratios (mean difference +79.3) and reduced mortality (RR 0.48), even in patients vulnerable to positional complications. Our review adds to this body of evidence by showing that prone positioning is feasible and safe in patients on ECMO support. Facial edema or catheter dislodgment were infrequent and did not differ between prone and supine groups. This supports a growing consensus that prone positioning extended safely to complex patient populations when performed under appropriate monitoring.

Our findings show the role of prone positioning not only as a therapeutic intervention but also as a prognostic tool. Several studies in our review, including Yan et al. (2025), linked oxygenation response post-proning to survival, which reinforce its utility in early clinical decision-making. While Schmidt et al. (2023) did not find significant differences in ECMO weaning rates, their results still suggested physiological improvements with prone positioning, consistent with other studies.

These findings strengthen the evidence base supporting prone positioning as a cornerstone in the management of moderate to severe ARDS. Despite variability in study design, the consistent improvements in oxygenation, ventilator days, and mortality in different populations affirm its clinical value. Future studies focus on patient stratification, optimal timing, and integration with advanced modalities should be encouraged to maximize outcomes.

CONCLUSION

Prone positioning is associated with improved oxygenation and in most of the included studies, and lower mortality when applied early and for extended durations. The intervention is feasible and safe even in patients on VV-ECMO. Response to prone positioning (measured by oxygenation improvement) is a strong prognostic marker for survival.

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Abbreviations

1) ARDS, Acute Respiratory Distress Syndrome
2) PaO_2/FiO_2, Arterial Partial Pressure of Oxygen to Fraction of Inspired Oxygen Ratio
3) ECMO, Extracorporeal Membrane Oxygenation
4) VV-ECMO, Veno-Venous Extracorporeal Membrane Oxygenation
5) RCT, Randomized Controlled Trial
6) PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses
7) ICU, Intensive Care Unit
8) PEEP, Positive End-Expiratory Pressure
9) PPV, Prone Position Ventilation
10) NOS, Newcastle-Ottawa Scale
11) COVID-19, Coronavirus Disease 2019
12) OR, Odds Ratio
13) RR, Relative Risk
14) CI, Confidence Interval
15) MV, Mechanical Ventilation

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