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Steroids in ARDS Management: A Review of Recent Advances and Clinical Guidelines

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Abstract: Acute Respiratory Distress Syndrome (ARDS) is one of the most daunting challenges in the field of critical care medicine, characterized by diffuse alveolar injury, severe hypoxemia, and high mortality rates despite the progress in mechanical ventilation and supportive care. The use of corticosteroids in the management of ARDS has been controversial in the past, with shifting attitudes being fuelled by recent clinical trials, meta-analyses, and empirical data, especially with the COVID-19 pandemic. Corticosteroids are presumed to modulate the dysregulated host response that lies at the core of ARDS, given their anti-inflammatory and antifibrotic effects. This narrative review embarks on a critical review of the pathophysiologic rationale for the use of steroids in ARDS, reviews landmark clinical studies that have shaped current clinical practice and distils recent guidelines by major health organizations. The review also explores heterogeneities in steroid responsiveness based on the timing of administration, etiology of ARDS, and the unique phenotypes of individual patients. Through the synthesis of the latest evidence, this article seeks to provide clinicians with an integrated view of the judicious use of steroids in ARDS while promoting an evidence-based approach to improve patient outcomes.

Keywords- Acute Respiratory Distress Syndrome, Corticosteroids, Methylprednisolone, Dexamethasone, Lung Inflammation, Cytokine Storm, Ventilatory Support, Clinical Practice Guidelines, COVID-19, Critical Care Pharmacotherapy

1. INTRODUCTION

Acute Respiratory Distress Syndrome (ARDS) is a serious condition that occurs commonly in intensive care units (ICUs), which the Berlin criteria define as the acute onset of hypoxemic respiratory failure with bilateral pulmonary infiltrates that are not completely explained by cardiac failure or fluid overload. Initially described in 1967 by Ashbaugh et al., ARDS continues to be a substantial cause of mortality and morbidity in the ICU, with an incidence of between 27% in mild forms and greater than 45% in severe ARDS [1]. Despite modern advances in strategies for mechanical ventilation, fluid administration, and critical care, the syndrome continues largely to lack reliable targeted pharmacologic therapies. The resultant high mortality and chronic morbidity highlight the importance of effective adjuvant treatment [2].

The pathophysiologic characteristic of ARDS is diffuse alveolar-capillary membrane injury as a result of a severe inflammatory insult. This is typically precipitated by conditions like severe pneumonia, aspiration, sepsis, pancreatitis, or massive blood transfusion. This leads to a cascade of immune dysregulation, neutrophilic infiltration, and discharge of pro-inflammatory cytokines including tumor necrosis factor-alpha (TNF-α), interleukin-1β, and interleukin-6. This results in enhanced vascular permeability, alveolar flooding, surfactant derangement, and decreased lung compliance. As the syndrome evolves through exudative, proliferative, and fibrotic stages, the chronic inflammation can progress to irreversible fibrosis, so it is important that intervention is prompt [3].

Corticosteroids, with their strong anti-inflammatory and immunosuppressive effects, have been suggested to counteract this dysregulated immune response. They act by inhibiting NF-κB activation, suppressing the release of pro-inflammatory cytokines, and enhancing alveolar fluid clearance. They can also possibly reduce the process of inflammation to fibrosis by regulating fibroblast proliferation and collagen deposition [4]. Although these are the mechanistic advantages, the clinical use of corticosteroids in ARDS has been controversial for a long time.

Early trials yielded conflicting results, with some instances indicating decrease in inflammatory markers and ventilator days, but others not demonstrating mortality benefit or even warning of impaired viral clearance delay and augmented secondary infections [5].

Traditionally, the timing, dosing, duration, and selection of corticosteroid have differed significantly between studies. The high-dose "pulse" regimens of the 1980s and 1990s were frequently linked with adverse effects, while more recent trials using lower, extended doses had better profiles of safety and efficacy. In contemporary times, focus has turned toward the administration of moderate-dose methylprednisolone or dexamethasone, especially when treatment is started early or in the intermediate course of ARDS. The publication of the DEXA-ARDS trial in 2020, followed by the RECOVERY trial amid the COVID-19 pandemic, represented a watershed moment for the corticosteroid controversy by illustrating an unequivocal mortality benefit in moderately to severely ill ARDS, especially when secondary to viral pneumonia [6].

The COVID-19 pandemic further emphasized the importance of corticosteroids in treating ARDS. ARDS became a leading cause of death among severe COVID-19 patients, prompted by an overactive host immune response or "cytokine storm." The administration of corticosteroids like dexamethasone was quickly proven in large-scale studies and included in global treatment guidelines. This clinical experience renewed interest in the use of corticosteroids in other etiologies of ARDS and led to revised recommendations by organizations like the World Health Organization (WHO), Surviving Sepsis Campaign (SSC), and the Society of Critical Care Medicine (SCCM) [7].

In the changing backdrop, it is essential that clinicians and researchers align new evidence with earlier controversies and further their comprehension of ideal corticosteroid use in ARDS. This review intends to discuss the mechanistic rationale, critically assess recent clinical trials, and integrate guideline-based recommendations for steroid application in ARDS. It also analyzes patient-specific variables like ARDS severity, disease phase, and host immune status that can affect response to corticosteroid therapy. Finally, the objective is to aid evidence-informed, patient-specific clinical decision-making in the management of ARDS with corticosteroids in contemporary critical care [8].

2. Pathophysiological Rationale for Steroid Use in ARDS

The pathogenesis of Acute Respiratory Distress Syndrome (ARDS) consists of a multifaceted interplay between inflammatory and immune-mediated pathways initiated by a primary lung insult or systemic inflammatory event. Appreciation of this cascade is needed to warrant and maximize the therapeutic application of corticosteroids in the treatment of ARDS [9].

ARDS progresses in three overlapping pathological stages: the exudative stage (days 1–7), the proliferative stage (days 7–14), and the fibrotic stage (after day 14). In the exudative stage, diffuse alveolar damage results from endothelial and epithelial injury. This results in heightened vascular permeability and the deposition of protein-rich fluid within the alveolar spaces, causing pulmonary edema, gas exchange impairment, and hypoxemia. This stage is marked by significant neutrophil recruitment, activation of alveolar macrophages, and the production of pro-inflammatory mediators such as interleukin (IL)-1β, IL-6, IL-8, and tumor necrosis factor-alpha (TNF-α) [10].

The proliferative phase is characterized by the activation of repair processes, type II pneumocyte proliferation, and the start of fibroblast activation. In case of uncontrolled or excessive inflammation, this phase leads to the fibrotic phase, which consists of extracellular matrix protein deposition, collagen, and permanent lung fibrosis. This leads to permanent pulmonary dysfunction and elevated mortality. It is this progression—from an acute inflammatory reaction to chronic fibrosis—that corticosteroids attempt to regulate [11].

Corticosteroids have their actions through interaction with intracellular glucocorticoid receptors (GRs), which are translocated into the nucleus and either inhibit pro-inflammatory gene expression (transrepression) or enhance anti-inflammatory gene transcription (transactivation). By inhibiting NF-κB and activator protein-1 (AP-1), corticosteroids suppress the generation of inflammatory cytokines, chemokines, adhesion molecules, and reactive oxygen species. Corticosteroids also increase the resolution of inflammation by enhancing apoptosis of activated immune cells and upregulating anti-inflammatory mediators such as IL-10 and annexin A1 [12].

In ARDS, corticosteroids stabilize endothelial and epithelial barriers, reconstitute alveolar fluid clearance by enhancing epithelial sodium channels and Na+/K+ ATPase activity, and suppress the activation of fibroblasts, thus constraining fibrotic evolution. In addition, corticosteroids can decrease the duration of mechanical ventilation by enhancing lung compliance and oxygenation [13].

Timing of steroid administration is a critical factor to consider. Early administration, preferably within 14 days of the onset of ARDS, has been associated with better outcomes, according to evidence. Fibroproliferative phase initiation may not be as effective or even counterproductive if there is already irreversible fibrosis. In addition, the choice of corticosteroid agent, dose, and duration needs to be carefully made to balance positive immunomodulation with potential immunosuppression, leading to secondary infections, hyperglycemia, and neuromuscular weakness [14].

In viral ARDS, as in COVID-19, the evidence for corticosteroid administration is also augmented by the presence of an overwhelming cytokine storm that is responsible for alveolar injury. In this setting, corticosteroids act to dampen the hyperinflammatory process and arrest further advancement of lung injury [15]. Yet, in viral infections such as influenza, the evidence is less certain owing to fears of compromised viral clearance and increased secondary bacterial pneumonia rates, calling for context-dependent use.

In conclusion, the case for the use of corticosteroids in ARDS is based on the central importance of inflammation in its pathophysiology. In modulation of the various arms of the inflammatory cascade, corticosteroids provide a biologically rational and clinically viable therapeutic strategy. Their ability to forestall fibroproliferative evolution, enhance ventilatory mechanics, and reduce ICU stay underpins current investigation and changing clinical practice [16].

3. Review of Key Clinical Trials and Evidence

The last two decades have seen multiple clinical trials test the effectiveness of corticosteroids in ARDS with a spectrum of results depending on differences in study design, steroid dose and type, timing of treatment, patient population, and etiology of ARDS. This paragraph outlines landmark trials and recent data that have influenced current clinical practice and conception about steroid therapy in ARDS [17].

3.1 Early Trials and Mixed Results

Early trials assessing corticosteroids in ARDS were controversial and uncertain. Bernard et al.'s (1987) study, one of the first randomized controlled trials (RCTs), examined high-dose methylprednisolone (30 mg/kg every 6 hours for 48 hours) in early ARDS and did not show benefit but with concerns of higher infection and gastrointestinal bleeding risk. These results clouded the use of steroids in ARDS for more than a decade [18].

Subsequently, Meduri et al. broke the paradigm by exploring the application of low-to-moderate doses of methylprednisolone for extended periods [19]. In a prospective 1998 study, they demonstrated improved oxygenation, decreased systemic inflammation, increased ventilator-free days, and a trend toward decreased mortality in patients who received methylprednisolone (2 mg/kg/day tapered over 28 days) at the initial fibroproliferative stage of ARDS. A 2007 ARDS Network trial tried to confirm these results but showed mixed outcomes [20]. Although methylprednisolone initiated after 7 days of ARDS improved lung function and decreased ICU stay, it did not decrease 60-day mortality significantly and was linked with higher risk of death when initiated after 14 days.

These initial trials emphasized two important principles: (1) the timing of corticosteroid administration is important, with earlier treatment tending to yield improved results; and (2) extremely high-dose steroids are likely to be dangerous and should be avoided in ARDS.

3.2 The DEXA-ARDS Trial (2020)

One of the most influential recent studies was the DEXA-ARDS trial, a multicenter RCT that took place in Spain and recruited 277 patients with moderate to severe ARDS (PaO_2/FiO_2 <200 mmHg) unconnected to COVID-19. Patients were given dexamethasone 20 mg/day for 5 days, followed by 10 mg/day for 5 days [21]. The study demonstrated a strong decrease in 60-day mortality (21% vs. 36% controls) and increased ventilator-free days (12.3 vs. 7.5). Notably, no rise in severe adverse events was noted, further supporting the safety and effectiveness of early, moderate-dose dexamethasone in non-COVID ARDS.

3.3 The RECOVERY Trial (2020) and COVID-19 ARDS

The RECOVERY trial was a turning point in the steroid-ARDS story. Carried out during the COVID-19 pandemic in the UK, this enormous adaptive RCT recruited more than 6,000 hospitalised patients with confirmed SARS-CoV-2 infection. In patients on oxygen or mechanical ventilation, dexamethasone 6 mg IV once daily for up to 10 days reduced 28-day mortality vs. standard care (22.9% vs. 25.7%). Conversely, no improvement was observed in those without respiratory support [22].

These results quickly changed the world treatment practices, and dexamethasone now became the standard of care in COVID-19-associated ARDS. The effect was most notable in invasive mechanical ventilation patients, serving as robust support for the effectiveness of corticosteroids in viral-induced ARDS with a hyperinflammatory phenotype.

4. Subsequent Meta-Analyses and Guidelines

To address the increasing evidence, the WHO REACT Working Group conducted a meta-analysis of 7 RCTs in 1,703 critically ill COVID-19 patients. It established that systemic corticosteroids decreased all-cause mortality compared to usual care or placebo (OR 0.66, 95% CI 0.53–0.82). Crucially, this advantage was maintained regardless of the steroid type (dexamethasone, hydrocortisone, methylprednisolone), lending class-effect benefits if appropriately utilized [23].

Outside of COVID-19, in a 2017 meta-analysis of 9 trials involving 1,371 ARDS patients by Ruan et al., corticosteroid treatment was linked to lower mortality (RR 0.75), higher PaO_2/FiO_2 ratio, and greater ventilator-free days, especially when given early in the course of disease.

4.1 Timing, Dose, and Duration Considerations

The best steroid regimen continues to be the subject of controversy. There is evidence favoring early treatment—ideally during the first 7 days after ARDS has developed. Late treatment is possibly less effective or harmful. Intermediate-dose regimens (e.g., dexamethasone 6–20 mg/day, methylprednisolone 1–2 mg/kg/day) administered for 7–10 days seem to provide the best efficacy-safety trade-off [24].

Increased doses and extended therapy are usually avoided with risks of immunosuppression, hyperglycemia, neuromyopathy, and secondary infections. Weaning should be done slowly to prevent rebound inflammation, especially in long-course therapy.

4.2 Real-World Observations and Phenotypic Variability

Post-RECOVERY real-world evidence has once again reminded us that all patients do not benefit equally. Sub phenotype studies indicate that hyperinflammatory ARDS (characterized by increased IL-6, ferritin, and CRP) is more responsive to steroids than hypoinflammatory subtypes. This provides promise for biomarker-guided treatment, where corticosteroids can be selectively given according to inflammatory profile rather than a one-size-fits-all strategy [25].

In conclusion, recent data firmly endorse the early administration of moderate-dose corticosteroids in severe to moderate ARDS, particularly of inflammatory or viral etiology. Studies such as DEXA-ARDS and RECOVERY have put an end to decades of debate and have informed major revisions in clinical guidelines worldwide.

5. Current Clinical Guidelines and Recommendations

As a result of the advent of strong evidence favoring corticosteroid use in moderate to severe ARDS, key health authorities and professional societies have updated their guidelines to mirror current best practices. Nonetheless, disagreement with recommendations remains, especially concerning non-COVID versus COVID ARDS, as well as regarding steroid option, dose, and duration.

5.1 Surviving Sepsis Campaign (SSC) Guidelines – COVID-19 (2020/2021)

- In response to the RECOVERY trial, the SSC, together with the Society of Critical Care Medicine (SCCM) and the European Society of Intensive Care Medicine (ESICM), provided strong recommendations supporting the use of corticosteroids in critically ill COVID-19 patients. The 2021 update suggests giving:
- Dexamethasone 6 mg IV or orally daily for a maximum of 10 days in patients needing supplemental oxygen or mechanical ventilation.
- In patients who cannot tolerate dexamethasone, doses of methylprednisolone or hydrocortisone that are equivalent can be administered.
- Steroids are not to be used routinely in non-hypoxemic or mildly ill patients with COVID-19.
- Guidelines recommended initiating therapy early in the course of secondary disease after hypoxemia has been achieved yet cautioned against prolonged immunosuppression and increased risks of secondary infections.

5.2 WHO Guidelines (2020–2023)

The World Health Organization (WHO), with its Rapid Evidence Appraisal for COVID-19 Therapies (REACT) Working Group, issued a strong recommendation of systemic corticosteroids in seriously ill COVID-19 patients. The guideline recommends:

- Dexamethasone 6 mg daily for 7–10 days as the preferred regimen.
- Alternate steroids such as methylprednisolone (32 mg/day) or hydrocortisone (160 mg/day) can be used if dexamethasone is unavailable.
- Corticosteroids are contraindicated in patients with non-severe COVID-19 not requiring respiratory support.

The WHO recognized a moderate degree of evidence for mortality benefit and emphasized the importance of individualized evaluation in low-resource environments, particularly where diagnostic distinction between bacterial and viral infections is poor.

5.3 Society of Critical Care Medicine (SCCM) – Non-COVID ARDS

In its recommendations for general ARDS management, the SCCM cautiously supports corticosteroid use, particularly when administered early:

- For early moderate-to-severe ARDS (PaO_2/FiO_2 <200 mmHg), methylprednisolone 1 mg/kg/day IV for 14 days, tapered gradually, is considered a reasonable option.
- Initiating steroids within 72 hours of ARDS diagnosis appears most beneficial.
- Prolonged use or initiation after day 14 is not recommended due to lack of benefit and possible harm.

SCCM also highlights the need for close monitoring of glycemic status, infection markers, and ventilator-associated complications.

5.4 European Society of Intensive Care Medicine (ESICM)

ESICM supports a patient-centered, individualized approach:

- Recommends early low-to-moderate dose corticosteroids in patients with elevated inflammatory biomarkers (e.g., CRP >150 mg/L, IL-6).
- Prefers dexamethasone or methylprednisolone depending on clinician familiarity and institutional protocol.
- Emphasizes tapering regimens over abrupt discontinuation, especially in patients treated longer than 7 days.

ESICM also advocates integrating steroids within a multimodal ARDS bundle that includes lung-protective ventilation, conservative fluid management, and prone positioning.

5.5 National Institutes of Health (NIH) Guidelines – COVID-19

The NIH COVID-19 Treatment Guidelines Panel recommends:

- **Dexamethasone 6 mg once daily for up to 10 days** in patients requiring mechanical ventilation or high-flow oxygen.
- In non-COVID ARDS, NIH does not provide a formal recommendation but acknowledges that dexamethasone may be beneficial in moderate-to-severe ARDS based on emerging trial data (e.g., DEXA-ARDS).

The NIH also cautions against combining corticosteroids with other immunomodulators unless in the setting of a controlled clinical trial or compelling clinical indication.

5.6 Indian Council of Medical Research (ICMR) & Ministry of Health Guidelines – India (2021 Update)

In the Indian context, corticosteroids were included in national COVID-19 treatment protocols based on RECOVERY findings. Recommendations include:

- **Dexamethasone 6 mg/day for 5–10 days** in moderate to severe COVID-19 with respiratory distress.
- Advises against steroid use in early/mild cases or without hypoxia.
- Emphasizes concurrent thromboprophylaxis and infection surveillance during steroid therapy.

6. Summary of Guideline Convergence and Divergence

Table 1. Summary of Guideline Convergence and Divergence

Guideline Body	Indication	Steroid Recommended	Dose	Duration	COVID-Specific
WHO	Severe/Critical COVID-19	Dexamethasone or equivalent	6 mg/day	7–10 days	Yes
SSC	Moderate-Severe COVID-19 ARDS	Dexamethasone	6 mg/day	Upto 10 days	Yes
SCCM	Non-COVID ARDS	Methylprednisolone	1 mg/kg/day	14 days tapered	No
ESICM	ARDS with inflammation	Dexamethasone or methylprednisolone	Individualized	7–14 days	Both
NIH	COVID-19 ARDS	Dexamethasone	6 mg/day	Upto 10 days	Yes
ICMR	COVID-19 (Moderate-Severe)	Dexamethasone	6 mg/day	5–10 days	Yes

In summary, clinical guidelines from leading global and regional bodies now **strongly support the use of corticosteroids in moderate to severe ARDS**, particularly when initiated early and guided by clinical severity and inflammatory markers. While dexamethasone has emerged as the most studied and preferred agent in COVID-19-related ARDS, methylprednisolone remains widely used in non-COVID ARDS, especially in early or fibroproliferative phases. Clinicians must tailor steroid therapy based on timing, severity, etiology, and individual patient risk profiles.

7. Clinical Considerations, Controversies, and Practical Pearls

Despite growing support for corticosteroid use in ARDS, particularly following the COVID-19 pandemic, several clinical uncertainties and controversies persist. The decision to initiate steroids in ARDS should always be contextualized within an individual patient's clinical status, disease phase, inflammatory phenotype, and overall risk-benefit profile. This section addresses critical real-world considerations, unresolved controversies, and key practical insights that can aid clinicians in applying evidence-based steroid therapy in ARDS management [26].

7.1 Timing of Initiation

Timing is a decisive factor in determining steroid efficacy. Evidence supports early administration—preferably within the first 72 hours of onset of moderate to severe ARDS. Early use targets the exudative inflammatory phase, where steroids can mitigate alveolar damage and prevent fibroproliferation. Delayed initiation beyond 14 days has shown limited or adverse outcomes, likely due to irreversible fibrotic changes already established in lung parenchyma [27].

Practical Tip: Initiate steroids as early as possible in patients with confirmed ARDS, particularly if inflammatory markers (CRP, IL-6) are elevated and mechanical ventilation is required.

7.2 Dose and Choice of Steroid

There is no universal consensus on the ideal corticosteroid or dose. However, recent studies favor **moderate dosing** strategies:

- **Dexamethasone**: 6–20 mg/day IV, most commonly used in viral ARDS.
- **Methylprednisolone**: 1–2 mg/kg/day IV in divided doses, preferred in non-COVID ARDS or cases with suspected fibrosis.
- **Hydrocortisone**: 200–400 mg/day IV, sometimes used for patients with septic shock and ARDS overlap.

High-dose regimens (>250 mg/day of methylprednisolone or dexamethasone equivalents) are associated with worse outcomes due to immunosuppression, hyperglycemia, and neuromuscular complications [28].

Practical Tip: Avoid "pulse" high-dose regimens. Use the lowest effective dose for the shortest necessary duration, with a tapering strategy when extending beyond 7–10 days.

7.3 Duration and Tapering

The ideal duration of corticosteroid therapy in ARDS varies with the severity and trajectory of disease. Most protocols recommend a **course of 7–10 days** for dexamethasone or up to 14 days for methylprednisolone, especially in non-resolving ARDS. Abrupt discontinuation after prolonged therapy (>5–7 days) may cause rebound inflammation and deterioration [19].

Practical Tip: For courses longer than 5 days, gradually taper steroids over 3–5 days or more based on patient stability and inflammatory markers.

7.4 Monitoring for Adverse Effects

Steroid therapy is not without risk. Common adverse effects include:

- **Hyperglycemia** (especially in diabetics or prolonged use)
- **Secondary infections** (bacterial/fungal), especially ventilator-associated pneumonia
- **Myopathy and neuromuscular weakness**
- **Delirium or psychiatric disturbances**
- **Electrolyte imbalances** (hypokalemia, fluid retention)

Practical Tip: Initiate tight glucose control, implement aggressive infection surveillance, and provide DVT prophylaxis. Monitor electrolytes and mental status during therapy

7.5 Special Populations and Contraindications

- **Immunocompromised patients**: Use with caution, weighing benefits against risk of reactivation of latent infections.
- **Patients with active fungal infections, tuberculosis, or uncontrolled diabetes**: Steroids may exacerbate underlying conditions and should be used judiciously.
- **Pregnant patients**: Use lowest effective dose; consider fetal impact.

Practical Tip: Screen for latent tuberculosis, fungal colonization, and prior immunosuppression before prolonged steroid therapy.

7.6 Phenotypic Targeting: The Future?

Emerging data suggest that not all ARDS patients benefit equally from steroids. Studies have identified hyperinflammatory and hypoinflammatory sub phenotypes, with the former demonstrating greater responsiveness to corticosteroids. Biomarkers such as IL-6, ferritin, and soluble TNF receptor-1 are under investigation to guide therapy [29].

Practical Tip: In the future, inflammatory biomarker panels may guide steroid use—consider steroids in patients with high CRP, ferritin, or IL-6 levels pending further validation.

7.7 Differentiating ARDS Etiologies

The response to corticosteroids may vary based on ARDS cause:

- **COVID-19 ARDS**: Strongest evidence for benefit with dexamethasone.
- **Bacterial pneumonia-related ARDS**: Steroids may mask infection or worsen it if not well-controlled.
- **Influenza-associated ARDS**: Controversial; some studies suggest harm, likely due to impaired viral clearance.

Practical Tip: Reserve steroids for ARDS of known or suspected inflammatory origin. Avoid routine use in influenza unless in cytokine storm or septic shock.

7.8 Integration with Other Therapies

Corticosteroids should not be considered in isolation but as part of a comprehensive ARDS management protocol including:

- Lung-protective ventilation (low tidal volume strategy)
- Prone positioning
- Conservative fluid therapy
- Neuromuscular blockade in select cases
- Early mobilization and nutrition

Practical Tip: Steroid therapy should enhance—not replace—core supportive ARDS management principles.

8. Conclusion

The role of corticosteroids in the management of Acute Respiratory Distress Syndrome has evolved significantly, transitioning from skepticism to evidence-backed endorsement, particularly in the wake of recent clinical trials and global experiences during the COVID-19 pandemic. Steroids have demonstrated the ability to attenuate excessive pulmonary inflammation, prevent fibroproliferative progression, reduce ventilator dependence, and improve survival in selected ARDS populations. Evidence now supports the early use of moderate-dose corticosteroids—especially dexamethasone and methylprednisolone—in patients with moderate to severe ARDS, provided they are carefully selected and closely monitored. However, their use remains nuanced, requiring consideration of timing, ARDS etiology, inflammatory phenotype, and individual patient risk factors. As the field progresses, future strategies may integrate biomarker-guided and phenotypic-based steroid therapy to further personalize care. Until then, clinicians must balance benefits against potential harms while adhering to evolving clinical guidelines and institutional protocols to optimize outcomes in ARDS patients.

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10. Conflicts of Interest

The authors declare no conflicts of interest.

11. REFERENCES

1. Diamond M, Peniston HL, Sanghavi DK, Mahapatra S. Acute Respiratory Distress Syndrome. [Updated 2024 Jan 31]. In: *StatPearls* [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan Available from: https://www.ncbi.nlm.nih.gov/books/NBK436002/
2. Horie S, McNicholas B, Rezoagli E, Pham T, Curley G, McAuley D, et al. Emerging pharmacological therapies for ARDS: COVID-19 and beyond. *Intensive Care Med*. 2020 Dec;46(12):2265-2283. https://doi.org/10.1007/s00134-020-06141-z
3. Sinha P, Bos LD. Pathophysiology of the Acute Respiratory Distress Syndrome: Insights from Clinical Studies. *Crit Care Clin*. 2021 Oct;37(4):795-815. https://doi.org/10.1016/j.ccc.2021.05.005
4. Yasir M, Goyal A, Sonthalia S. Corticosteroid Adverse Effects. In: *StatPearls* [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan. Available from: https://www.ncbi.nlm.nih.gov/books/NBK531462/
5. Landolf KM, Lemieux SM, Rose C, Johnston JP, Adams CD, Altshuler J, et al. Corticosteroid use in ARDS and its application to evolving therapeutics for coronavirus disease 2019 (COVID-19): A systematic review. *Pharmacotherapy*. 2022 Jan;42(1):71-90. https://doi.org/10.1002/phar.2637
6. Hahn D, Hodson EM, Willis NS, Craig JC. Corticosteroid therapy for nephrotic syndrome in children. *Cochrane Database Syst Rev*. 2015 Mar 18;2015(3):CD001533. https://doi.org/10.1002/14651858.cd001533.pub5
7. van Paassen J, Vos JS, Hoekstra EM, Neumann KMI, Boot PC, Arbous SM. Corticosteroid use in COVID-19 patients: a systematic review and meta-analysis on clinical outcomes. *Crit Care*. 2020 Dec 14;24(1):696. https://doi.org/10.1186/s13054-020-03400-9
8. Khilnani GC, Hadda V. Corticosteroids and ARDS: A review of treatment and prevention evidence. *Lung India*. 2011 Apr;28(2):114-9. https://doi.org/10.4103/0970-2113.80324
9. Swenson KE, Swenson ER. Pathophysiology of Acute Respiratory Distress Syndrome and COVID-19 Lung Injury. *Crit Care Clin*. 2021 Oct;37(4):749-776. https://doi.org/10.1016/j.ccc.2021.05.003
10. Matthay MA, Zemans RL. The acute respiratory distress syndrome: pathogenesis and treatment. *Annu Rev Pathol*. 2011;6:147-63. https://doi.org/10.1146/annurev-pathol-011110-130158
11. Savin IA, Zenkova MA, Sen'kova AV. Pulmonary Fibrosis as a Result of Acute Lung Inflammation: Molecular Mechanisms, Relevant In Vivo Models, Prognostic and Therapeutic Approaches. *Int J Mol Sci*. 2022 Nov 29;23(23):14959. https://doi.org/10.3390/ijms232314959
12. Nicolaides NC, Chrousos G, Kino T. Glucocorticoid Receptor. [Updated 2020 Nov 21]. In: Feingold KR, Ahmed SF, Anawalt B, et al., editors. *Endotext* [Internet]. South Dartmouth (MA): MDText.com, Inc.; 2000-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK279171/
13. Jayasimhan D, Matthay MA. Corticosteroids in adults with acute respiratory distress syndrome and severe pneumonia. *BJA Educ*. 2023 Dec;23(12):456-463. https://doi.org/10.1016/j.bjae.2023.08.005
14. Kuperminc E, Heming N, Carlos M, Annane D. Corticosteroids in ARDS. *J Clin Med*. 2023 May 8;12(9):3340. https://doi.org/10.3390/jcm12093340
15. Lin SH, Zhao YS, Zhou DX, Zhou FC, Xu F. Coronavirus disease 2019 (COVID-19): cytokine storms, hyper-inflammatory phenotypes, and acute respiratory distress syndrome. *Genes Dis*. 2020 Dec;7(4):520-527. https://doi.org/10.1016/j.gendis.2020.06.009
16. Zhou K, Qin Q, Lu J. Pathophysiological mechanisms of ARDS: a narrative review from molecular to organ-level perspectives. *Respir Res*. 2025 Feb 13;26(1):54.https://doi.org/10.1186/s12931-025-03137-5
17. Li G, Chen D, Gao F, Huang W, Wang J, Li Y, et al. Efficacy of corticosteroids in patients with acute respiratory distress syndrome: a meta-analysis. *Ann Med*. 2024 Dec;56(1):2381086. https://doi.org/10.1080/07853890.2024.2381086
18. Bernard GR, Luce JM, Sprung CL, Rinaldo JE, Tate RM, Sibbald WJ, et al. High-dose corticosteroids in patients with the adult respiratory distress syndrome. *N Engl J Med*. 1987 Dec 17;317(25):1565-70. https://doi.org/10.1056/nejm198712173172504
19. Meduri GU, Siemieniuk RAC, Ness RA, Seyler SJ. Prolonged low-dose methylprednisolone treatment is highly effective in reducing duration of mechanical ventilation and mortality in patients with ARDS. *J Intensive Care*. 2018 Aug 24;6:53. https://doi.org/10.1186/s40560-018-0321-9
20. Wajanaponsan N, Reade MC, Milbrandt EB. Steroids in late ARDS? *Crit Care*. 2007;11(4):310. https://doi.org/10.1186/cc5954
21. Villar J, Ferrando C, Martínez D, Ambrós A, Muñoz T, Soler JA, et al. Dexamethasone treatment for the acute respiratory distress syndrome: a multicentre, randomised controlled trial. *Lancet Respir Med*. 2020 Mar;8(3):267-276. https://doi.org/10.1016/s2213-2600(19)30417-5
22. Matthay MA, Thompson BT. Dexamethasone in hospitalised patients with COVID-19: addressing uncertainties. *Lancet Respir Med*. 2020 Dec;8(12):1170-1172. https://doi.org/10.1016/s2213-2600(20)30503-8
23. Ma S, Xu C, Liu S, Sun X, Li R, Mao M, et al. Efficacy and safety of systematic corticosteroids among severe COVID-19 patients: a systematic review and meta-analysis of randomized controlled trials. *Signal Transduct Target Ther*. 2021 Feb 21;6(1):83. http://dx.doi.org/10.1038/s41392-021-00521-7
24. Yoshihro S, Taito S, Yatabe T. The influence of steroid type on outcomes in patients with acute respiratory distress syndrome. *J Intensive Care*. 2023 Jul 10;11(1):32 https://doi.org/10.1186/s40560-023-00681-4

25. Torres LK, Siempos II. Identifying a hyperinflammatory subphenotype of ARDS associated with worse outcomes: may ferritin help? *Thorax*. 2024 Feb 15;79(3):200-201. https://doi.org/10.1136/thorax-2023-221131
26. Chaudhuri D, Sasaki K, Karkar A, Sharif S, Lewis K, Mammen MJ, et al. Corticosteroids in COVID-19 and non-COVID-19 ARDS: a systematic review and meta-analysis. *Intensive Care Med*. 2021 May;47(5):521-537. https://doi.org/10.1007/s00134-021-06394-2
27. Hirano Y, Madokoro S, Kondo Y, Okamoto K, Tanaka H. Corticosteroid treatment for early acute respiratory distress syndrome: a systematic review and meta-analysis of randomized trials. *J Intensive Care*. 2020 Dec 7;8(1):91 https://doi.org/10.1186/s40560-020-00510-y
28. Ocejo A, Correa R. Methylprednisolone. [Updated 2024 Aug 11]. In: *StatPearls* [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK544340/
29. Sinha P, Furfaro D, Cummings MJ, Abrams D, Delucchi K, Maddali MV, et al. Latent Class Analysis Reveals COVID-19-related Acute Respiratory Distress Syndrome Subgroups with Differential Responses to Corticosteroids. *Am J Respir Crit Care Med*. 2021 Dec 1;204(11):1274-1285. https://doi.org/10.1164/rccm.202105-1302oc