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Research Article

Early Corticosteroids in Severe ARDS: A Step Forward

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Abstract

Background: The severe form of acute respiratory failure known as acute respiratory distress syndrome (ARDS) is brought on by disruption to the alveolar barrier and increased permeability of pulmonary capillaries, which results in pulmonary edema and poor gas exchange. It is caused by a complicated inflammatory response and frequently arises because of illnesses like sepsis or pneumonia. Effective treatment is still difficult despite improvements in ventilation and hydration management; corticosteroids show promise because of their anti-inflammatory and anti-fibrotic properties.

Methods: This randomized controlled experiment was carried out in the general closed intensive care unit (ICU) at Kobba Medical Compound utilizing a straightforward randomization technique. Patients with severe ARDS who were hospitalized to the intensive care unit were included in the study. Participants were divided into two groups at random: Group 1 was given an early infusion of 100 mg of methylprednisolone per day to treat severe ARDS, while Group 2 was given the conventional treatment regimen without methylprednisolone.

Results: When comparing the Methylprednisolone group to the Placebo group, the outcome analysis shows a substantial decrease in the length of mechanical ventilation and ICU stay. Methylprednisolone-treated patients needed mechanical ventilation for considerably fewer days (8.91±1.83 vs. 10.38±3.15 days, p=0.009), indicating a quicker recovery and possible improvement in respiratory function. Furthermore, the Methylprednisolone group's ICU stay was considerably shorter (10.23 ±2.02 vs. 11.50 ±3.08 days, p =0.025), suggesting a faster stabilization overall. Methylprednisolone improves recovery metrics; however, it may not have a substantial effect on survival rates, as seen by the comparable death rates between the groups (59.1% alive in the Methylprednisolone group vs. 54.5% in the Placebo group, p=0.667).

Conclusion: The findings showed that early methylprednisolone therapy in severe ARDS can enhance recovery metrics, such as ventilator-free days and ICU stay, indicating a quick recovery and stability of organ function. The lack of a discernible effect on death, however, emphasizes how difficult it is to manage ARDS and how little Corticosteroids may increase survival. To further clarify the possible function of methylprednisolone in the treatment of ARDS, more research with bigger sample sizes, longer follow-up times, and earlier corticosteroid Administration is required.

Keywords: Corticosteroids, ARDS, ICU, PEEP, TRALI, Methylprednisolone.

Key message

- Methylprednisolone does not significantly lower mortality rates, indicating that while it improves short-term recovery metrics, it may not affect overall survival outcomes.

- More extensive research is required to clarify the ideal timing, dosage, and long-term benefits of Corticosteroid therapy in the management of severe ARDS.
- Early methylprednisolone administration in severe ARDS significantly reduces the duration of mechanical ventilation and ICU stay, indicating faster recovery and improved respiratory function.

Introductions

A kind of acute hypoxemic respiratory failure known as acute respiratory distress syndrome (ARDS) is characterized by pulmonary edema brought on by increased permeability of the alveolar epithelial and pulmonary capillary endothelial cells. Diffuse alveolar injury, which happens during the acute or exudative phase of ARDS, substantially impairs gas exchange and compromises lung compliance by disrupting lung barrier function [1]. ARDS may be caused by acute pulmonary inflammation, which includes a variety of inflammatory cells and mediators. With its strong anti-inflammatory and anti-fibrotic properties, corticosteroids may help treat ARDS [2].

The dangerous illness known as acute respiratory distress syndrome (ARDS) is defined as refractory hypoxemia brought on by a few reasons and typically results from several lung diseases or extrapulmonary disorders, including pneumonia, drowning, and non-pulmonary sepsis. Particularly in youngsters, it may result in respiratory failure, serious sickness, or even death. According to a prior study, 10.4% of patients in need of ICU care are thought to have ARDS [3]. Effective treatment of ARDS is still difficult because of two factors like tidal volume, high positive end-expiratory pressure, advanced infection, and fewer medications, even though mechanical ventilation and fluid management have recently shown their effectiveness [4].

ARDS is a common reaction to several causes. Alveolar-capillary damage is the first stage of ARDS, followed by a proliferative phase with better lung function and repair, and a final fibrotic phase that marks the conclusion of the acute illness process. Inflammation, apoptosis, necrosis, and enhanced alveolar-capillary permeability are the hallmarks of pulmonary epithelial and endothelial cellular injury, which results in alveolar edema and proteinosis. Hypoxemia results from reduced gas exchange brought on by alveolar edema. The non-uniformity of the damage pattern observed in ARDS is one of its defining characteristics [5]. Reduced regional lung compliance, which typically affects the bases more than the apices, may occur from more severe lung segment damage. Intrapulmonary differential in pathology results in a variant response to oxygenation strategies, such as increased positive end-expiratory pressure (PEEP), which may improve oxygen diffusion in affected alveoli but may cause volutrauma and atelectrauma of adjacent unaffected alveoli. Ultimately, this injury manifests as impaired gas exchange, decreased lung compliance, and pulmonary hypertension [6]. About 10% of patients in intensive care units worldwide have ARDS, which is primarily caused by pneumonia, sepsis, aspiration of stomach contents, or severe trauma. In most studies, mortality is still high at 30–40%, despite

significant improvements. Diffuse alveolar damage is often seen in pathological specimens from ARDS patients, and laboratory research has shown lung endothelial and alveolar epithelial damage, which leads to the buildup of Protein-rich inflammatory edematous fluid in the alveolar space. Consensus syndromes are used for diagnosis, with adjustments made for settings with limited resources [7].

Pneumonia (bacterial and viral; fungal is less common), non-pulmonary sepsis, aspiration of stomach and/or oral and esophageal contents (which may be worsened by subsequent infection), and significant trauma are the most common conditions in which ARDS develop. Acute pancreatitis, transfusions of fresh frozen plasma, red blood cells, and/or platelets, drug overdoses with various agents, near drowning, hemorrhagic shock or reperfusion injury, and smoke inhalation are a few other less frequent situations that are linked to the development of ARDS [8].

Patients with refractory sepsis or community-acquired pneumonia, as well as those whose ARDS have been triggered by therapies, such as low tidal volume ventilation, most patients with persistent or refractory moderate to severe ARDS are relatively early in the disease course (within 14 days of onset with a PaO2/FiO2 ratio <200 mm Hg), [9,10]. Glucocorticoids can also be used to manage these patients. However, patients with less severe ARDS or those whose ARDS last longer than 14 days are typically not prescribed glucocorticoids. Additionally, patients with some viral diseases, like influenza, have worse outcomes when using them [11]. Methylprednisolone has been seen as a potentially useful treatment. It is one of the most significant physiological inhibitors of inflammation and an end-effector of the hypothalamic-pituitary-adrenal axis. Hundreds of genes involved in stress-related homeostasis may be impacted. At the cellular level, cytoplasmic heat shock protein–complexed glucocorticoid receptors are activated by methylprednisolone. Moreover, it interacts with active nuclear factor-kB to inhibit DNA binding and subsequent transcriptional activity. However, mental adverse events, iatrogenic Cushing syndrome, infections, and osteoporosis are among the side effects of methylprednisolone that may outweigh its therapeutic benefits [12]. As Severe ARDS is a life-threatening lung injury where fluid accumulates in the lungs, making breathing extremely difficult. Severe ARDS is characterized by excessive inflammation throughout the body. Researchers anticipated that early administration of methylprednisolone during severe ARDS

would: Reduce the body's inflammatory response, potentially reducing lungs and other organ damage. Better oxygen exchange and a speedier recovery from ARDS could result from improved lung function. Decreased complications: Lower levels of inflammation may result in fewer problems including infections and organ failure, which would improve patient outcomes in general. This study aims to show whether methyl prednisolone might affect those patients' outcomes. This study compared the effects of early methyl prednisolone infusion on oxygenation, ventilator-free days, and mortality rates in patients with severe ARDS. a steroid-responsive disease, may receive glucocorticoids.

Patient And Methods

Study design and patient setting

Using a straightforward randomization technique, this investigation was planned as a randomized controlled experiment. Patients admitted to the intensive care unit (ICU) with a confirmed diagnosis of severe ARDS were included in the study, which took place in the general closed ICU at Kobba Medical Compound during the period of the study.

Ethical consideration statement

All participating patients' guardians were asked for their written informed consent after being fully informed about the study's specifics, including the nature of the studies. The Research Ethics Committee at AFCM, Egypt, has authorized the study procedure, which was carried out in compliance with the Declaration of Helsinki's ethical guidelines.

Patients' selection criteria

Patients who required intubation with mechanical ventilation, had severe ARDS (PaO_2/FiO_2 ≤100 mm Hg), and acquired acute respiratory distress syndrome (ARDS) within 72 hours after the onset of their chest ailment were eligible for inclusion. Patients with a medical history of interstitial lung disease, corticosteroid therapy administered within seven days prior to admission, or any contraindications to corticosteroid usage were excluded.

Sample size estimation

Patients were recruited using a straightforward non-probability sampling technique. Based on previous data from [13], which reported means of 16.5 ± 10.1 versus 8.7±10.2 days ($p<0.001$), the sample size was determined by comparing mechanical ventilation–free days by day 28 between patients with severe ARDS treated with methylprednisolone versus placebo. A minimum of 74 patients with severe ARDS, split equally between the two groups, were needed to reach a power of 90% and a significance threshold of 0.05. The overall sample size was expanded to 88 patients, with 44 patients allocated to each group, to account for an expected dropout rate of 20%.

All patients were subjected to:

Age, sex, body mass index, admission date, and prior medical and surgical history were all recorded in the patient's complete medical history. Vital signs at admission, the Sequential Organ Failure Assessment (SOFA) score [14], the partial pressure of oxygen to fraction of inspired oxygen ratio (PaO_2/FiO_2), and the indication, mode, and initial settings of mechanical ventilation were all included in the clinical evaluation.

Complete blood count (CBC), serum albumin, C-reactive protein (CRP), arterial blood gases (ABG), and lactic Acid levels were among the laboratory tests.Acute onset, bilateral non-cardiogenic lung infiltrates seen on a chest X-ray, CT scan, or ultrasound, and moderate to severe oxygenation impairment (defined as $PaO_2/FiO_2 \leq 300$ mm Hg or $SaO_2/FiO_2 \leq 315$ when oxygen saturation measured by pulse oximetry is ≤ 97%) were used to diagnose ARDS. To distinguish ARDS from other causes of acute respiratory failure, including pulmonary edema, pulmonary embolism, pneumonia, COPD, asthma, and pneumothorax, bedside lung ultrasonography using the BLUE protocol, a quick (less than three minutes) diagnostic tool, was used [15].

Based on its etiology, ARDS was further categorized as either extrapulmonary or pulmonary. The Berlin definition of severity was used: mild (PaO_2/FiO_2 200–300 mm Hg), moderate (100–199 mm Hg), or severe (<100 mm Hg) [16]. ABG analysis was used to calculate PaO_2/FiO_2 ratios, with FiO_2 represented as a decimal (0.21–1). For instance, a patient on 80% oxygen ($FiO_2 = 0.8$) with a PaO_2 of 100 mm Hg has a PaO_2/FiO_2 ratio of 125 mm Hg. Mechanical ventilation was the first line of treatment for severe ARDS, with additional techniques including neuromuscular blockade, extracorporeal membrane oxygenation (ECMO), or inhaled nitric oxide when needed. Using a pressure control volume-guarantee mode on a Dräger ventilator, each patient received the identical lung recruitment procedure with high positive end-expiratory pressure (PEEP), low tidal volume (6 mL/kg), and an increased respiratory rate to maximize oxygenation.

Intervention and Follow-up

Patients with severe ARDS were divided into two groups at random. Group 2 received conventional care without corticosteroids, while Group 1 had an early infusion of 100 mg of methylprednisolone per day. Identification and treatment of the underlying cause of ARDS, central venous and arterial line insertion, and ventilatory support with endotracheal intubation utilizing lung-protective techniques were all part of the standard treatment approach. Low tidal volumes (6 mL/kg of estimated body weight) were used for ventilation, and plateau pressures were kept below 30 cm H2O. If pressures were higher than 30 cm H2O, they could be adjusted to 4 mL/kg. To guarantee sufficient minute ventilation, respiratory rates were adjusted to allow for hypercapnia if PH remained

more than 7.30. Clinical discretion was used to apply positive end-expiratory pressure (PEEP), which may be beneficial in cases of moderate-to-severe ARDS.

Neuromuscular blocking and sedation were utilized to maximize ventilator synchrony in patients with PaO_2/FiO_2<150 mm Hg, and prone positioning was used for 16 consecutive hours per day in patients intubated for less than 36 hours, which has been demonstrated to lower mortality and enable early extubation. Treatment remained mainly supportive while treating the underlying problem; no pharmaceutical medication has been shown to improve results. Lung ultrasonography (LUS) was used to evaluate extravascular lung water, radiologic abnormalities, PaO_2/FiO_2 ratios, and the clinical course. Using a VIVID S5 digital ultrasound equipment and a phased-array probe (1.3–4 MHz), LUS was carried out using a predetermined 12-zone protocol that examined anterior, anterolateral, and posterior thoracic regions in the semi-recumbent position [17].

Outcomes of the study

Outcomes between the two groups were compared to evaluating the effect of methylprednisolone on recovery and clinical parameters in patients with severe ARDS.

Statistical analysis methods

IBM SPSS Statistics version 26.0 (SPSS Inc., Chicago, IL, USA) was used to analyze the data. Non-normally distributed variables were expressed as median with interquartile range (IQR), whereas quantitative variables with A normal distribution was provided as mean ± standard deviation (SD) and range. Counts and percentages were used to display qualitative variables. The Shapiro-Wilk and Kolmogorov-Smirnov tests were used to determine whether the data was normal. The independent samples t-test was used to compare two means, and the chi-square test was used to compare categorical variables. A 5% significance level and a 95% confidence interval were used. P-values were significant if $p < 0.05$, highly significant if $p < 0.01$, and not significant if $p > 0.05$.

Results

A flowchart of the study of 93 patients confirmed diagnosis of severe ARDS were enrolled in the current study, 5 patients were excluded from the study (3 patients declined consent, and 2 did not meet the inclusion criteria). So, 88 severe ARDS patients participated in the study and statically analyzed, 44 of them received an early methylprednisolone infusion at a dose of 100 mg daily (group A), and 44 other patients received standard treatment without corticosteroids (group B), (Figure 1).

This table 1 presents a comparison of baseline characteristics between the Methylprednisolone and Placebo groups, ensuring that both groups are comparable before intervention. The distribution of sex shows a slightly higher proportion of males in the Methylprednisolone group (59.1%) compared to the Placebo group (50%), though the difference is not statistically significant (p =0.392). Similarly, the mean age and BMI between the groups are closely matched, with no significant differences (p = 0.339 and p = 0.894, respectively), compares the prevalence of common comorbidities between the Methylprednisolone and Placebo groups. Hypertension, diabetes mellitus, and combinations of chronic conditions appear evenly distributed, with no statistically significant differences between the groups (p = 0.795). The proportion of patients with hypertension alone (18.2% vs. 15.9%), diabetes alone (15.9% in both groups), and combined conditions, including chronic obstructive pulmonary disease (COPD) or ischemic heart disease (IHD), show minor variations but remain statistically insignificant and the baseline vital signs of participants in the Methylprednisolone and Placebo groups, showing no statistically significant differences between them. Mean systolic and diastolic blood pressures are nearly identical (p = 0.680 and p = 0.578, respectively), indicating similar baseline cardiovascular status. Likewise, heart rate and respiratory rates show no meaningful variation between groups (p = 0.958 and p = 0.776, respectively), reinforcing the homogeneity of the study population (Table 1).

		Methylprednisolone e (n=44)		Placebo (n=44)		t	P- value
Systolic blood pressure	Mean ±SD	106.15 ± 11.89		105.25 ± 9.33		0.171	0.680
	Range	82 – 130		91 – 123			
Diastolic blood pressure	Mean ±SD	69.0 ± 8.26		69.95 ± 7.77		0.311	0.578
	Range	47 – 84		51 – 87			
Heart rate	Mean ±SD	113.81 ± 10.36		113.70 ± 9.74		0.034	0.958
	Range	98 – 130		99 – 130			
Respiratory rate	Mean ±SD	28.06 ± 5.57		27.75 ± 4.86		0.081	0.776
	Range	20 – 35		20 – 35			
Sex	Male	26	59.1	22	50.0	0.733	0.392
	Female	18	40.9	22	50.0		

Age	Mean ±SD	66.79 ± 7.01		68.29 ± 7.59		0.926	0.339
	Range	55 – 80		55 – 80			
BMI	Mean ±SD	26.54 ± 2.04		26.49 ± 1.61		0.018	0.894
	Range	21.6 – 31.2		23.4 – 29.2			
Hypertension		8	18.2	7	15.9	0.267	0.795
Diabetes mellitus		7	15.9	7	15.9		
HTN and DM		4	9.1	5	11.4		
HTN, DM, and COPD		16	36.4	17	38.6		
HTN, DM, IHD		9	20.5	8	18.2		

Using Independent test to compare between means, X2= Chi- Square test, p-value >0.05 is insignificant; *p-value <0.05 is significant; **p-value <0.01 is highly significant.

Table 1. Comparative Analysis of Patients' Demographics in Methylprednisolone and Placebo Groups.

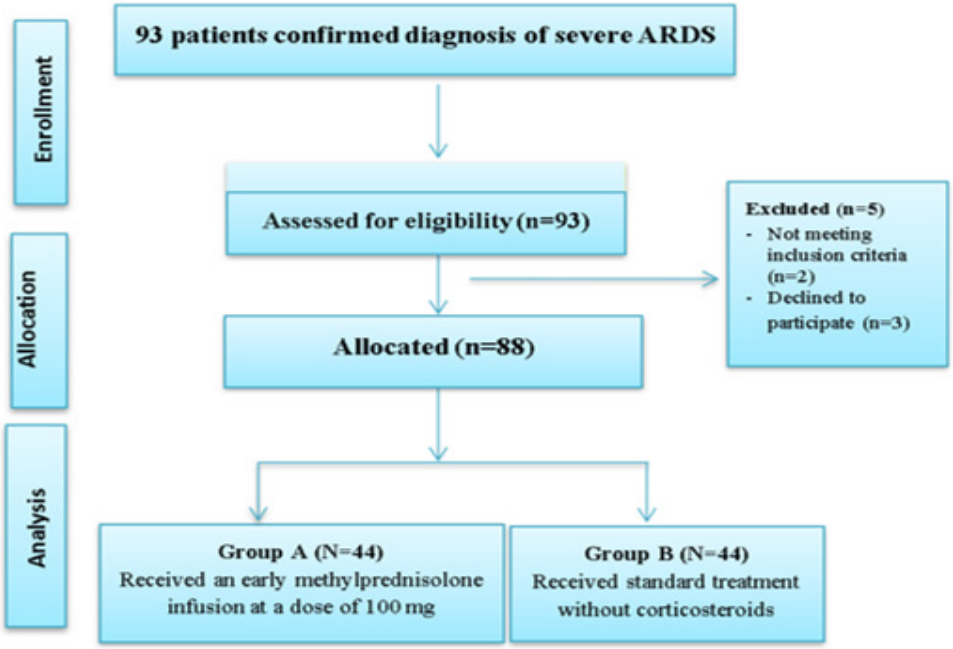

Figure 1: Flowchart of the studied patients' groups

The current study showed that, 2 presents a comparison of baseline laboratory parameters between the Methylprednisolone and Placebo groups, confirming the similarity of both cohorts. Hemoglobin levels, platelet counts, and total leukocyte counts are nearly identical, with no statistically significant differences (p = 0.692, p = 0.531, and p = 0.884, respectively). Albumin, creatinine, and inflammatory marker C-reactive protein (CRP) levels also show no significant variation, ensuring comparable nutritional and renal function statuses across groups. Similarly, Glasgow Coma Scale (GCS) scores, as well as CO_2 and O_2 levels, are consistent between groups (Table 2).

		Methylprednisolone (n=44)	Placebo (n=44)	t	P- value
Hemoglobin	Mean ±SD	9.06 ± 1.03	8.98 ± 0.90	0.158	0.692
	Range	6.70 – 10.9	7.20 – 11.1		
Platelet	Mean ±SD	204.5 ± 51.78	198.0 ± 45.98	0.396	0.531
	Range	85 – 324	36 – 274		

Total Leukocytes	Mean ±SD	13.22 ± 5.64	13.45 ± 5.12	0.039	0.884
	Range	4 – 22	4 – 21		
Albumin	Mean ±SD	3.0 ± 0.20	2.99 ± 0.22	0.065	0.800
	Range	2.6 – 3.4	2.5 – 3.5		
C-Reactive Protein	Mean ±SD	146.0 ± 35.42	142.5 ± 33.11	0.235	0.629
	Range	82 – 199	88 – 194		
Creatinine	Mean ±SD	2.05 ± 0.45	2.0 ± 0.36	0.083	0.775
	Range	1.0 – 3.4	1.2 – 2.9		
GCS	Mean ±SD	13.97 ± 0.90	13.95 ± 0.81	0.016	0.901
	Range	13 – 15	13 – 15		
CO2	Mean ±SD	73.09 ± 10.56	71.68 ± 11.69	0.352	0.555
	Range	55 – 90	56 – 90		
O2	Mean ±SD	75.59 ± 2.86	74.65 ± 2.95	2.255	0.137
	Range	70 – 80	70 – 80		

Using: Independent test to compare between means, X2= Chi- Square test, p-value >0.05 is insignificant; *p-value <0.05 is significant; **p-value <0.01 is highly significant.

Table 2. Comparative analysis of patients' laboratory findings in methylprednisolone and placebo groups.

In the present study there are no statistically significant differences between the methylprednisolone and placebo groups regarding severity scores and respiratory function parameters, the lung ultrasound score, sequential organ failure assessment (SOFA) Score, and acute physiology and chronic health evaluation (APACHE) score are closely matched, with p-values of 0.528, 0.872, and 0.168, respectively, confirming comparable disease severity in both groups. The PaO_2/FiO_2 ratio, a key marker of respiratory function, also shows no significant difference (p=0.432), a comparative follow-up analysis of patients on day 3 in the Methylprednisolone and Placebo groups, showing mixed results regarding early therapeutic effects. While the lung ultrasound scores and PaO_2/FiO_2 ratios remain statistically similar (p=0.122 and p=0.605, respectively), the APACHE score demonstrates a significant increase in the Methylprednisolone group (p=0.002), suggesting potential early fluctuations in disease severity. However, SOFA scores remain unchanged between groups (p = 0.797), indicating comparable organ dysfunction progression. ARDS severity also shows no notable differences, with the vast majority of patients in both groups classified as severe (Table 3). The follow-up data on day 7 demonstrates a significant clinical improvement in the Methylprednisolone group compared to the Placebo group. Both the SOFA and APACHE scores show highly significant reductions in the Methylprednisolone group ($p < 0.001$ for both), indicating a marked improvement in organ function and overall disease severity. Although the lung ultrasound scores trend lower in the Methylprednisolone group, the difference remains statistically insignificant (p=0.160). Oxygenation, as reflected by the PaO_2/FiO_2 ratio, remains comparable between groups (p=0.794), suggesting that while systemic severity improves; respiratory function shows no immediate advantage.ARDS severity classification also remains similar between groups, with nearly half of the patients recovering from ARDS (No ARDS: 45.5% vs. 43.2%, p=0.941), (Table 3).

		Methylprednisolone one (n=44)		**Placebo (n=44)**		**t**	**P-value**
		N	%	N	%		
Lung ultrasound Score	Mean ±SD	2.54 ± 0.50		2.47 ± 0.50		0.402	0.528
	Range	2 – 3		2 – 3			
SOFA Score	Mean ±SD	13.09 ± 1.82		13.15 ± 2.12		0.026	0.872
	Range	10 – 16		10 – 16			
APACHE Score	Mean ±SD	17.11 ± 1.96		16.54 ± 1.86		1.937	0.168
	Range	14 – 20		14 – 20			
PaO2/FiO2	Mean ±SD	70.56 ± 10.98		68.29 ± 11.25		0.622	0.432
	Range	51 – 90		50.3 – 88.3			

ARDS Severity	Mild (200-300)	0	0	0	0	-	-
	Moderate (100-199)	0	0	0	0		
	Severe (<100)	44	100	44	100		
Lung ultrasound Score	Mean ±SD	2.47 ± 0.62		2.68 ± 0.60		2.43	0.122
	Range	2 – 4		2 – 4			
SOFA Score	Mean ±SD	13.11 ± 2.12		13.22 ± 2.01		0.06	0.797
	Range	10 – 18		10 – 18			
APACHE Score	Mean ±SD	17.54 ± 1.67		16.18 ± 2.20		10.67	0.002**
	Range	14 – 20		12 – 20			
PaO2/FiO2	Mean ±SD	76.78 ± 18.80		78.68 ±15.40		0.26	0.605
	Range	51 – 150		50 – 130			
ARDS Severity	Mild (200-300)	0	0	0	0	0.21	0.645
	Moderate (100-199)	3	6.8	2	4.5		
	Severe (<100)	41	93.2	42	95.5		
Lung ultrasound Score	Mean ±SD	2.11 ± 1.36		2.52 ± 1.33		2.01	0.160
	Range	0 – 4		1 – 4			
SOFA Score	Mean ±SD	8.63 ± 7.05		14.05 ± 2.58		22.78	<0.001 **
	Range	2 – 19		10 – 19			
APACHE Score	Mean ±SD	10.02 ± 4.76		13.59 ± 5.16		11.33	<0.001 **
	Range	5 – 18		5 – 20			
PaO2/FiO2	Mean ±SD	205.90 ±119.85		199.09 ±123.98		0.069	0.794
	Range	60 – 360		60 – 370			
ARDS Severity	No ARDS (>300)	20	45.5	19	43.2	0.39	0.941
	Mild (200-300)	3	6.8	4	9.1		
	Moderate (100-199)	3	6.8	2	4.5		
	Severe (<100)	18	40.9	19	43.2		

Using: Independent t test to compare between means, X2= Chi- Square test, p-value >0.05 is insignificant; *p-value <0.05 is significant; **p-value <0.01 is highly significant.

Table 3. Baseline severity scores, respiratory function, follow up (day 3) and follow up (day 7) in methylprednisolone and placebo groups.

This table 4 highlights the mean differences in key clinical indicators between the Methylprednisolone and Placebo groups, showing a significant advantage for Methylprednisolone in reducing disease severity. Both the SOFA and APACHE scores improved significantly in the Methylprednisolone group compared to the Placebo group (p<0.001 for both), reflecting better organ function and overall patient stabilization. The lung ultrasound score showed a greater reduction in the Methylprednisolone group, but the difference was not statistically significant (p = 0.514), suggesting that lung recovery trends similarly in both groups. The PaO_2/FiO_2 ratio decreased comparably in both groups (p = 0.734), indicating that oxygenation status did not differ significantly despite systemic improvements (Table 4).

		Methylprednisolone (n=44)	**Placebo (n=44)**	**Test value**	**P-value**
Lung ultrasound Score	Mean ±SD	-0.43 ± 1.45	-0.05 ± 1.42	0.78	0.514
	Range	-2 – -1	-1 – 1		
SOFA Score	Mean ±SD	-4.46 ± 7.28	-0.90 ± 3.34	10.64	<0.001**
	Range	-8 – -3	-3 – 0		
APACHE Score	Mean ±SD	-7.09 ± 5.15	-2.95 ± 5.48	15.36	<0.001**
	Range	-9 – -2	-9 – 0		

PaO2/FiO2	Mean ±SD	-135.34 ± 120.35	-130.8±124.49	0.39	0.734
	Range	-270 – -9	-261.7 – -9		

Using: Independent test to compare between means, X2= Chi- Square test, p-value >0.05 is insignificant; *p-value <0.05 is significant; **p-value <0.01 is highly significant.

Table 4. Mean Difference in Severity Scores and Respiratory Function in Methylprednisolone and Placebo Groups

The outcome analysis demonstrates a significant reduction in the duration of mechanical ventilation and ICU stay in the Methylprednisolone group compared to the Placebo group. Patients receiving Methylprednisolone required significantly fewer days on mechanical ventilation (8.91 ± 1.83 vs. 10.38±3.15 days, p=0.009), suggesting a faster recovery and potential improvement in respiratory function. Additionally, ICU length of stay was significantly shorter in the Methylprednisolone group (10.23 ±2.02 vs. 11.50 ±3.08 days, p=0.025), indicating an overall quicker stabilization. However, mortality rates remained comparable between groups (59.1% alive in the Methylprednisolone group vs. 54.5% in the Placebo group, p 0.667), suggesting that while Methylprednisolone enhances recovery metrics, it may not significantly impact survival rates (Table 5).

		Methylprednisolone (n=44)		Placebo (n=44)		t	P-value
		N	%	N	%		
Mechanical Ventilator (Day)	Mean ±SD	8.91 ± 1.83		10.38 ± 3.15		7.218	0.009**
	Range	6 – 12		6 – 20			
Length of ICU (Day)	Mean ±SD	10.23 ± 2.02		11.50 ± 3.08		5.241	0.025*
	Range	8 – 18		8 – 22			
Mortality	Alive	26		59.1		0.185	0.667
	Dead	18		40.9			

Using: Independent test to compare between means, X2= Chi- Square test, p-value >0.05 is insignificant; *p-value <0.05 is significant; **p-value <0.01 is highly significant.

Table 5. Outcome among methylprednisolone and placebo groups.

The Kaplan-Meier survival curve shows a higher cumulative survival probability in the methylprednisolone group compared to the placebo group over time. The survival curves diverge, with the placebo group experiencing a steeper decline, reaching zero survival by day 20. Censoring marks indicate ongoing follow-up in both groups, with more censored cases in the methylprednisolone group, suggesting longer survival. This pattern implies a potential survival benefit of methylprednisolone (Figure 2).

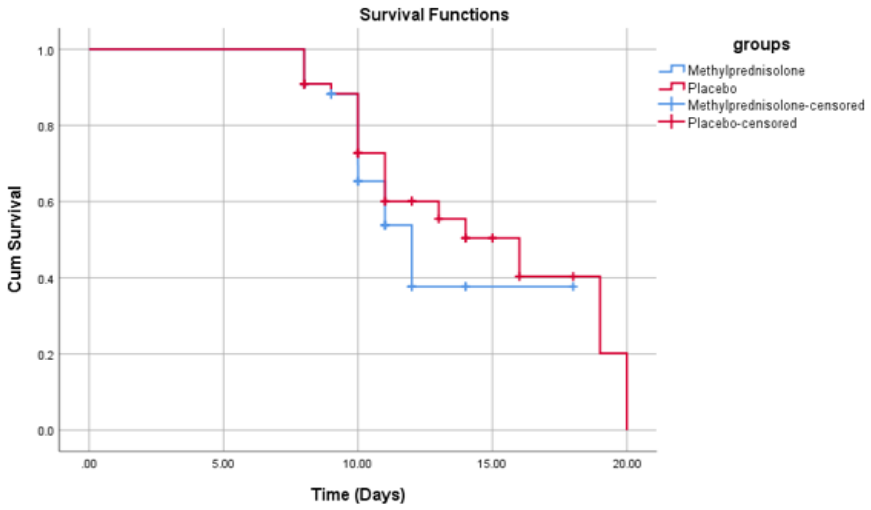

Figure 2. Kaplan-Meier survival analysis of methylprednisolone vs. placebo.

Discussion

Widespread lung damage and inflammation are hallmarks of severe ARDS, a potentially fatal illness that frequently results in respiratory failure [1]. Numerous factors, such as infections, trauma, and other systemic diseases can cause it. According to [18], ARDS is frequently linked to a high death rate and necessitates substantial medical intervention, including mechanical ventilation and supportive treatment. ARDS is a crucial disease for both early detection and treatment since its severity is correlated with the degree of pulmonary inflammation and alveolar destruction [19]. Because of its strong anti- inflammatory and immunosuppressive qualities, methylprednisolone, a corticosteroid, is frequently used to treat a variety of inflammatory and autoimmune diseases [20]. The role of early corticosteroid therapy, particularly methylprednisolone, in ARDS has been investigated in recent studies [21]. Methylprednisolone's capacity to control the inflammatory response, lower cytokine release, and possibly stop More lung damage is the justification for its use in ARDS. There has been continuous discussion and research on its usage in ARDS, especially in the early stages [3].

This study's main goal was to assess the efficacy of early methylprednisolone infusion in patients with severe ARDS, with an emphasis on enhancing important clinical outcomes such ventilator-free days, length of ICU stays, and overall disease severity. The results of participants receiving methylprednisolone and those getting a placebo were compared in the study. The findings warrant a thorough examination since they show both notable advancements and restrictions in the therapeutic use of methylprednisolone in ARDS patients. The two groups had similar demographics, comorbidities, vital signs, and laboratory results at baseline. This is a crucial component of randomized controlled trials because it guarantees that the intervention, not confounding variables, is responsible for any variations in clinical results.

In this instance, both groups shared similar characteristics, including age, sex, BMI, and concomitant illnesses like diabetes and hypertension. By reducing the influence of pre-existing disparities, the lack of significant variances in these baseline characteristics strengthens the validity of the study's conclusions. In ARDS, a disorder that is frequently exacerbated by comorbidities including diabetes, Hypertension, and cardiovascular disease, this matching is particularly crucial. These disorders are common in critically sick patients and can have an independent impact on ARDS prognosis. According to earlier research, individuals with ARDS who also have comorbid conditions like diabetes or hypertension may experience worse results, such as longer hospitalizations in the intensive care unit and greater death rates. A study by [22] found that Increased inflammation in ARDS was linked to concomitant diabetes mellitus, which may impair clinical outcomes. The current investigation successfully isolates the effect of methylprednisolone by guaranteeing comparable baseline features between the methylprednisolone and placebo groups, which is necessary for deriving reliable conclusions [23,24,5]. The PaO_2/FiO_2 ratio, lung ultrasonography scores, and established severity scores like SOFA and APACHE are among the clinical and laboratory parameters used to evaluate the severity of ARDS. These assessments showed no significant differences between the groups at baseline, suggesting that both groups had comparable illness severity upon admission. This is crucial because it guarantees that the groups start the study in similar circumstances, enabling a more reliable comparison of results following intervention. However, by Day 7, the methylprednisolone group's SOFA and APACHE scores had significantly improved following the drug's treatment. Both the SOFA score, which measures the degree of organ failure, and the APACHE score, which gauges the severity of illness and mortality risk, significantly improved in the methylprednisolone group, suggesting a possible decrease in organ dysfunction and systemic inflammation. These findings are consistent with earlier research showing how corticosteroids help critically ill patients by lowering systemic inflammation, which enhances organ performance. According to [13], methylprednisolone infusion significantly reduced lung injury score (LIS) and improved SOFA scores in early ARDS, suggesting decreased organ damage. Moreover, [25] also highlighted that Corticosteroids, such as methylprednisolone, lowered mortality and the SOFA score in ARDS patients. These results lend credence to the theory that corticosteroids, such as methylprednisolone, can assist stabilize organ function in ARDS by reducing the systemic inflammatory response. Nevertheless, there was no statistically significant difference between the two groups' lung ultrasonography ratings despite these improvements in systemic markers of inflammation. This implies that although methylprednisolone seems to enhance organ function and systemic inflammation, pulmonary function and lung repair do not significantly increase right away [9,10].

This finding aligns with some studies that suggest corticosteroids primarily reduce inflammation but may have limited direct effects on the structural and functional recovery of the lungs in ARDS. [26,25] both report that although corticosteroids can reduce inflammatory indicators, they don't always result in appreciable increases in lung compliance or oxygenation. [26] found that In ARDS patients, corticosteroids reduced systemic inflammation but did not directly improve lung compliance or oxygenation. This suggests that the main benefit of corticosteroids may be in reducing systemic inflammation rather than pulmonary inflammation. In contrast, in conditions like pneumonia, where inflammation has a more localized impact in lung injury, corticosteroids may directly speed up lung healing [27,28].

The study's main conclusion is that patients on methylpred-

nisolone had shorter ICU stays and less time on mechanical ventilation. Patients in the methylprednisolone group required mechanical breathing for an average of 8.91 days as opposed to 10.38 days in the placebo group. In a similar vein, the methylprednisolone group's average ICU stay was 10.23 days, which was considerably less than the placebo group's 11.50 days. These variations imply that early methylprednisolone infusion may speed up the stabilization of severely ill ARDS patients, enabling a quicker weaning off mechanical breathing and ICU release [29-32]. The methylprednisolone group's reduced mechanical breathing duration may be explained by the medication's anti-inflammatory properties. One of the main characteristics of ARDS is inflammation, which is known to be reduced by corticosteroids, such as methylprednisolone. Methylprednisolone may assist in improving lung compliance and oxygenation by lowering pulmonary edema, fibrosis, and other inflammatory reactions. This would ultimately enhance respiratory performance and lessen the requirement for mechanical ventilation.

This aligns with the findings of [13], where ARDS patients who received a lengthier methylprednisolone infusion experienced a faster extubation because their lung inflammation decreased. Because a shorter ICU stay is linked to a lower risk of hospital-acquired infections, complications, and medical expenses, it is especially crucial for managing ARDS. Long-term ICU admissions have been shown to increase the risk of secondary infections, such as ventilator-associated pneumonia, as well as other problems like delirium and muscle weakness, which can impede recovery and lengthen hospital stays [33,34]. Therefore, the methylprednisolone group's shorter ICU stay is a clinically meaningful result that demonstrates the medication's ability to hasten recovery in situations of severe ARDS. Numerous investigations on corticosteroid therapy in ARDS are in line with these results. [26] found that Corticosteroids have the potential to improve the overall management of ARDS because they not only shortened the duration of mechanical ventilation but also decreased the length of stay in the intensive care unit and enhanced recovery times. Similarly, [22] demonstrated that Methylprednisolone reduced ICU stays and increased ventilator-free days in ARDS patients. The mortality rate did not change significantly between the two groups despite improvements in clinical outcomes, such as shorter ICU stays and shorter durations of mechanical ventilation. There was no statistically significant difference between the death rates in the methyl prednisolone group (40.9%) and the placebo group (45.5%). This implies that methylprednisolone does not seem to have a significant impact on survival rates in this patient population, even though it may hasten recovery and enhance organ function in ARDS patients.

This result is consistent with prior research that looked at corticosteroids' effect in ARDS. Corticosteroids have been found to improve recovery measures like ventilator-free days and ICU duration of stay, although their effect on long-term survival is still debatable. [25,26] both found Despite improvements in short-term outcomes like the length of mechanical ventilation, there is no discernible survival benefit with corticosteroid therapy in ARDS patients. The timing of methylprednisolone delivery may be one reason why there was no survival benefit in this research. Since the corticosteroid treatment was started after severe ARDS developed, it might not have been the best time to increase survival. Early corticosteroid therapy in ARDS, especially in the early stages of the illness, may improve survival results, according to a few studies. For instance, [26] found that When corticosteroid medication was started within 72 hours of the onset of ARDS, mortality rates were reduced more than when it was administered later. It's also crucial to remember that the pathophysiology of ARDS might differ depending on its underlying cause, such as sepsis, trauma, or pneumonia, and that these variables may have an impact on how well corticosteroids work. [25,26] pointed out that Certain subtypes of ARDS, such as pneumonia-related ARDS, where inflammation is more localized, may benefit more from corticosteroid therapy.

According to the study's findings, early methylprednisolone infusion may have a major positive impact on recovery indicators like ventilator-free days and ICU stay duration. However, care should be taken when interpreting these advancements. They show that methyl prednisolone may hasten recovery in individuals with severe ARDS, but they do not imply that the medication improves survival. When determining whether to administer methylprednisolone to patients with severe ARDS who are already getting the best possible supportive treatment, clinicians should take these findings into account. The possible adverse effects of corticosteroid therapy, such as elevated risk of infections, delayed wound healing, and hyperglycemia, must also be taken into consideration. The extensive use of corticosteroids in ARDS patients, particularly those who are already critically sick and at risk of complications, may be restricted by these side effects.

Strength and limitations of the study

Several limitations should be noted, even if this trial offers insightful information on the possible advantages of methylprednisolone in severe ARDS. First, the results may not be as applicable in different contexts because the study was carried out in a single-center intensive care unit. Second, the statistical power to identify minute variations, especially in mortality outcomes, may be diminished by the very small sample size (44 patients per group). Lastly, the fact that methylprednisolone was given after severe ARDS had started may have limited its effect on long-term survival; an earlier intervention might have produced different outcomes.

Conclusion

This study concludes that early methylprednisolone therapy

in severe ARDS may enhance recovery measures, such as ventilator-free days and ICU stay, indicating quicker recovery and stability of organ function. The lack of a discernible effect on death, however, emphasizes how difficult it is to manage ARDS and how little corticosteroids may do to increase survival. To further clarify the possible function of methylprednisolone in the treatment of ARDS, more research with bigger sample sizes, longer follow-up times, and earlier corticosteroid administration is required.

Declaration

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Availability of data and material: All data supporting the study are presented in the manuscript or available upon request.

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