

## The role of baseline PaO<sub>2</sub>/FiO<sub>2</sub>, SpO<sub>2</sub> and IL-6 indicators in predicting in-hospital mortality in ARDS patients: a retrospective cohort study

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**Abstract** The aim of this study was to evaluate the role of baseline oxygenation parameters, including PaO<sub>2</sub>/FiO<sub>2</sub> and SpO<sub>2</sub>, as well as the inflammatory marker IL-6, in predicting in-hospital mortality among patients treated in the intensive care unit with a diagnosis of acute respiratory distress syndrome (ARDS). Low baseline PaO<sub>2</sub>/FiO<sub>2</sub> and SpO<sub>2</sub> levels and elevated IL-6 values are strongly associated with in-hospital mortality in patients with ARDS. The combined use of oxygenation parameters and IL-6 may provide a simple, accessible, and clinically useful approach for early mortality risk stratification in intensive care settings.

**Keywords:** ARDS; Mortality; PaO<sub>2</sub>/FiO<sub>2</sub>; Oxygen Saturation; Interleukin-6; Intensive Care Units

## 1. Introduction

Acute respiratory distress syndrome (ARDS) and severe viral pneumonias, especially those associated with COVID-19, are characterized by high mortality, and early risk assessment plays an important role in clinical decision-making [1]. Hypoxemia and systemic inflammatory response are considered the main pathophysiological mechanisms in the course of the disease, and these processes are closely associated with oxygenation indices and cytokine levels [2].

The PaO<sub>2</sub>/FiO<sub>2</sub> ratio is one of the most widely used indicators in assessing the severity of ARDS, and low levels have been associated with high mortality [3]. Various studies have shown that the PaO<sub>2</sub>/FiO<sub>2</sub> measured at admission is an independent prognostic factor for both short-term and 28-day mortality [4]. At the same time, dynamic changes in PaO<sub>2</sub>/FiO<sub>2</sub> have also been associated with patient survival probability [5].

The SpO<sub>2</sub>/FiO<sub>2</sub> ratio is a non-invasive indicator that can be used as an alternative to arterial blood gas analysis and shows a strong correlation with PaO<sub>2</sub>/FiO<sub>2</sub> [6]. Studies have shown that SpO<sub>2</sub>/FiO<sub>2</sub> is useful both in assessing disease severity and predicting mortality [7]. In addition, combining this parameter with other clinical scores further increases prognostic accuracy [8].

Among inflammatory biomarkers, interleukin-6 (IL-6) is of particular importance. Elevated IL-6 levels are

associated with a “cytokine storm,” which may lead to the development of ARDS and multi-organ failure [9]. Clinical studies have shown that high IL-6 levels are directly associated with an increased risk of mortality [10]. Furthermore, when IL-6 and PaO<sub>2</sub>/FiO<sub>2</sub> are used together, higher accuracy in mortality prediction is achieved [11].

In modern approaches, constructing risk models using a combination of several biomarkers is considered more effective. For example, multivariable models including SpO<sub>2</sub>/FiO<sub>2</sub>, IL-6 and other laboratory indicators have demonstrated high discriminative ability [12]. At the same time, adding clinical factors such as age and comorbidities to these models further increases their prognostic value [13].

However, most existing studies have evaluated the role of individual biomarkers separately, while their combined use and application in specific populations have not been sufficiently studied. Therefore, comprehensive evaluation of the role of admission PaO<sub>2</sub>/FiO<sub>2</sub>, SpO<sub>2</sub> and IL-6 in predicting mortality remains insufficiently investigated.

The aim of this study is to evaluate the relationship between baseline oxygenation indicators and inflammatory markers with mortality in ARDS patients and to investigate the construction of a prognostic model based on these parameters.

## 2. Methods

This study was conducted as a retrospective, single-center cohort study. The study was carried out based on the medical records of patients with acute respiratory distress syndrome (ARDS) who were treated in the intensive care unit of Baku Medical Plaza, Babek branch.

The main objective of the study was to evaluate the role of oxygenation parameters recorded during hospitalization and the level of IL-6, an inflammatory biomarker, in predicting in-hospital mortality in patients with ARDS. In this study, the effect of treatment was not evaluated; rather, the relationship between the patient's initial clinical-biological profile and the risk of death was investigated.

Patients aged 18 years and older who were treated in the intensive care unit with a diagnosis of ARDS were included in the study. The diagnosis of ARDS was determined based on the Berlin criteria. Only patients who had PaO<sub>2</sub>/FiO<sub>2</sub>, SpO<sub>2</sub>, and IL-6 parameters available during hospitalization were included in the analysis.

#### Inclusion criteria:

- being 18 years of age or older;
- presence of a diagnosis of ARDS;
- availability of initial PaO<sub>2</sub>/FiO<sub>2</sub>, SpO<sub>2</sub>, and IL-6 results;
- known in-hospital clinical outcome.

#### Exclusion criteria:

- patients younger than 18 years of age;
- absence of essential respiratory or laboratory parameters;
- incomplete information regarding clinical outcome;
- insufficient information in medical records for analysis.

All data were collected retrospectively from the patients' electronic and written medical records. The collected data included demographic parameters, clinical characteristics, comorbidities, respiratory parameters, laboratory results, and in-hospital outcome.

Demographic and clinical variables included age, sex, arterial hypertension, diabetes mellitus, chronic lung disease, smoking history, and length of stay in the intensive care unit.

The biomarkers and respiratory parameters selected for the main analysis were as follows:

- PaO<sub>2</sub>/FiO<sub>2</sub> ratio;
- SpO<sub>2</sub> parameter;
- SpO<sub>2</sub>/FiO<sub>2</sub> ratio;
- IL-6 level.

PaO<sub>2</sub>/FiO<sub>2</sub> was calculated as the ratio of the partial pressure of oxygen in arterial blood to the fraction of inspired oxygen. SpO<sub>2</sub>/FiO<sub>2</sub> was calculated based on the ratio of peripheral oxygen saturation to FiO<sub>2</sub>. IL-6 level was recorded based on laboratory analysis results obtained during hospitalization.

Only baseline parameters were used in this study. Serial changes and post-treatment dynamics were not included in the main analysis, because the purpose of the study was to assess the risk of death based on baseline clinical-biological parameters.

The primary endpoint of the study was defined as in-hospital mortality. Patients were divided into two groups according to final outcome:

- surviving patients;
- patients who died during hospitalization.

In the main analysis, the differences in baseline PaO<sub>2</sub>/FiO<sub>2</sub>, SpO<sub>2</sub>/FiO<sub>2</sub>, SpO<sub>2</sub>, and IL-6 parameters between these two groups were evaluated.

A prognostic model was constructed based on baseline oxygenation and inflammatory markers to assess mortality risk. Initially, PaO<sub>2</sub>/FiO<sub>2</sub>, SpO<sub>2</sub>/FiO<sub>2</sub>, and IL-6 parameters were included in the model. Later, the addition of clinical variables such as age, sex, and major comorbidities to the model was considered.

The purpose of the model was to divide patients into higher- and lower-risk groups in terms of risk of death. Therefore, both the prognostic power of individual biomarkers and that of the combined model were evaluated separately in the analysis.

Due to the retrospective design, some clinical and laboratory parameters may have been incomplete in certain patients. Patients

without PaO<sub>2</sub>/FiO<sub>2</sub>, SpO<sub>2</sub>, and IL-6 parameters, which were essential for the main analysis, were excluded from the analysis. Missing data for other variables were recorded separately, and statistical analyses were performed based on available data.

Data imputation was not performed. This approach was chosen in accordance with the nature of the retrospective study.

Statistical analyses were performed using IBM SPSS Statistics version 29.0. The distribution of continuous variables was assessed using appropriate normality tests and visual methods. Non-normally distributed continuous variables were presented as median and interquartile range (Q1–Q3), while categorical variables were presented as number and percentage (%). Comparison of continuous variables between surviving and deceased patients was performed using the Mann–Whitney U test, and comparison of categorical variables was performed using the chi-square test or Fisher’s exact test where appropriate.

To evaluate the relationship between baseline PaO<sub>2</sub>/FiO<sub>2</sub>, SpO<sub>2</sub>, and IL-6 parameters and in-hospital mortality, univariable logistic regression analysis was first performed. Clinically significant variables and variables with  $p < 0.10$  in the univariable analysis were included in the multivariable logistic regression model. PaO<sub>2</sub>/FiO<sub>2</sub>, SpO<sub>2</sub>, and IL-6 were included in the main prognostic analysis. Demographic characteristics and comorbidities, including age, sex, arterial hypertension, diabetes mellitus, chronic lung

disease, and smoking status, were reviewed as part of the baseline clinical profile and considered in the clinical interpretation of the findings. Since IL-6 had a right-skewed distribution, it was used in log-transformed form in the analyses. Results were presented with odds ratio (OR), 95% confidence interval (CI), and p value.

The ability of prognostic parameters to discriminate mortality was evaluated by receiver operating characteristic (ROC) analysis. Area under the curve (AUC), optimal cut-off values, sensitivity, and specificity were calculated for PaO<sub>2</sub>/FiO<sub>2</sub>, SpO<sub>2</sub>, and IL-6. Optimal cut-off values were determined based on the Youden index. In addition, a combined prognostic model including PaO<sub>2</sub>/FiO<sub>2</sub>, SpO<sub>2</sub>, and IL-6 together was constructed, and its discrimination ability was compared with individual parameters. Model discrimination was evaluated using ROC analysis and AUC values. Because of the retrospective single-center design and limited sample size, formal calibration analysis and external validation were not performed. Therefore, the combined model was interpreted mainly according to its discrimination performance, and future studies should assess calibration using methods such as the Hosmer–Lemeshow goodness-of-fit test and calibration plots.

This study was conducted based on the retrospective analysis of medical data of patients treated at Baku Medical Plaza, Babek branch. The study protocol was approved by the Medical Plaza Ethics Committee (Protocol number: BMP-06-

2025; approval date: 18 June 2025). The study was carried out in accordance with the principles of the Declaration of Helsinki. Due to the retrospective design, individual written consent was not obtained from the patients; all data were anonymized and patient confidentiality was protected.

### 3. Results

A total of 97 ARDS patients with complete baseline PaO<sub>2</sub>/FiO<sub>2</sub>, SpO<sub>2</sub>, and IL-6 parameters were included in the study. Of the patients, 58 survived, while 39 died during hospitalization. Overall in-hospital mortality was 40.2%. Marked differences were observed between surviving and deceased patients in terms of baseline oxygenation parameters and inflammatory marker levels.

PaO<sub>2</sub>/FiO<sub>2</sub> was significantly lower in deceased patients compared with surviving patients. While the median PaO<sub>2</sub>/FiO<sub>2</sub> in survivors was 180.0 (165.0–190.0), this parameter was 128.0 (107.0–140.0) in deceased patients, and the difference was statistically significant ( $p < 0.001$ ). This result shows that the risk of death is higher in patients with more severe oxygenation impairment at baseline.

The SpO<sub>2</sub> parameter changed in a similar direction. The median baseline SpO<sub>2</sub> was 88.0% (87.0–90.0) in surviving patients and 81.0% (80.0–82.5) in deceased patients. The difference between the groups was statistically significant ( $p < 0.001$ ). This result shows that SpO<sub>2</sub>, a simple and non-invasive

parameter, may also be useful in initial risk assessment in patients with ARDS.

IL-6 levels were higher in deceased patients. The median IL-6 was determined as 936.5 (861.5–959.5) in survivors and 1025.0 (965.0–1082.0) in deceased patients ( $p < 0.001$ ). This result shows that a high systemic inflammatory response is associated with in-hospital mortality.

The duration of intensive care was longer in surviving patients. The median duration of intensive care was 14.0 days (11.0–16.0) in survivors and 9.0 days (6.0–13.5) in deceased patients ( $p < 0.001$ ). This difference may indicate that clinical deterioration occurred earlier in deceased patients.

The comparison of baseline clinical-laboratory parameters between surviving and deceased patients is presented in Table 1, and the visual distribution of these parameters by groups is presented in Figure 2.

Figure 2. Comparison of baseline parameters in surviving and deceased patients.

Baseline PaO<sub>2</sub>/FiO<sub>2</sub>, SpO<sub>2</sub>, and IL-6 parameters were compared between surviving and deceased patients and are presented in Figure 2.

In logistic regression analysis, PaO<sub>2</sub>/FiO<sub>2</sub>, SpO<sub>2</sub>, and IL-6 parameters showed a statistically significant association with in-hospital mortality. Each 10-unit increase in PaO<sub>2</sub>/FiO<sub>2</sub> was associated with a decrease in the probability of death (OR=0.35; 95% CI:

0.23–0.53;  $p < 0.001$ ). Each 1% increase in SpO<sub>2</sub> was also associated with a decrease in mortality risk (OR=0.57; 95% CI: 0.47–0.69;  $p < 0.001$ ). Conversely, each 100-unit increase in IL-6 level increased the probability of death (OR=10.92; 95% CI: 3.96–30.16;  $p < 0.001$ ).

In multivariable analysis, when PaO<sub>2</sub>/FiO<sub>2</sub> and IL-6 were evaluated together, both parameters retained their association with mortality. Each 10-unit increase in PaO<sub>2</sub>/FiO<sub>2</sub> reduced the risk of death (OR=0.41; 95% CI: 0.27–0.63;  $p < 0.001$ ), while each 100-unit increase in IL-6 increased the risk of death (OR=4.02; 95% CI: 1.30–12.37;  $p = 0.015$ ). When SpO<sub>2</sub> was added to the model, the overall prognostic performance of the combined model increased, although the independent effect of SpO<sub>2</sub> was at the borderline level of significance ( $p = 0.071$ ). This may be explained by the close clinical relationship between SpO<sub>2</sub> and PaO<sub>2</sub>/FiO<sub>2</sub> parameters.

The results of logistic regression and ROC analysis for variables associated with mortality are shown in Table 2.

In ROC analysis, the highest discrimination ability among individual parameters was observed for PaO<sub>2</sub>/FiO<sub>2</sub> (AUC=0.944). The AUC was 0.911 for SpO<sub>2</sub> and 0.868 for IL-6. The optimal cut-off was determined as  $\leq 150$  for PaO<sub>2</sub>/FiO<sub>2</sub>,  $\leq 86\%$  for SpO<sub>2</sub>, and  $\geq 976$  for IL-6. In the combined model, when PaO<sub>2</sub>/FiO<sub>2</sub> and IL-6 were used together, the AUC was 0.951. When PaO<sub>2</sub>/FiO<sub>2</sub>, SpO<sub>2</sub>, and IL-6 were included in the model together,

the AUC increased to 0.962. This result shows that the combined biomarker approach provides higher prognostic accuracy compared with individual parameters.

The ability of PaO<sub>2</sub>/FiO<sub>2</sub>, SpO<sub>2</sub>, IL-6, and the combined model to discriminate mortality is presented in Figure 1, and the distribution of the probability of death calculated based on the combined model among surviving and deceased patients is presented in Figure 3.

Table 1. Comparison of baseline parameters between survivors and non-survivors

Parameter	Survivors (n=58)	Non-survivors (n=39)	p value
PaO <sub>2</sub> /FiO <sub>2</sub>	180.0 (165.0–190.0)	128.0 (107.0–140.0)	<0.001
SpO <sub>2</sub> , %	88.0 (87.0–90.0)	81.0 (80.0–82.5)	<0.001
IL-6	936.5 (861.5–959.5)	1025.0 (965.0–1082.0)	<0.001
ICU stay, days	14.0 (11.0–16.0)	9.0 (6.0–13.5)	<0.001

Table 2. Construction of the prognostic model and mortality-associated variables

Model variable	Odds Ratio	95% CI	p value	Adjusted Odds Ratio	Optimal Cut-off	Sensitivity	Specificity
PaO <sub>2</sub> /FiO <sub>2</sub>	0.3	0.2–0.5	<0.001	0.3	≤150	87%	94%
SpO <sub>2</sub>	0.5	0.4–0.7	<0.001	0.5	≥96%	92%	84%
IL-6	1.0	0.9–1.1	<0.001	1.0	≥906	69%	91%
PaO <sub>2</sub> /FiO <sub>2</sub> + IL-6 model	—	—	<0.001	—	—	87%	98%

+	6
SpO <sub>2</sub> +	2
IL-6	
model	

Figure 1. ROC curves for mortality prediction. The ability of PaO<sub>2</sub>/FiO<sub>2</sub>, SpO<sub>2</sub>, IL-6, and the combined model to discriminate mortality was evaluated using ROC analysis and is presented in Figure 1.

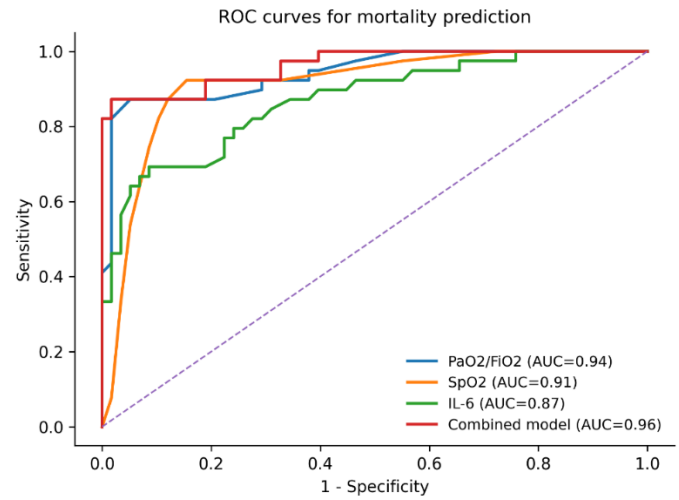


Figure 1.

Figure 2. Comparison of baseline parameters between survivors and non-survivors. Baseline PaO<sub>2</sub>/FiO<sub>2</sub>, SpO<sub>2</sub>, and IL-6 values were compared between survivors and non-survivors and are presented in Figure 2.

Baseline markers by outcome

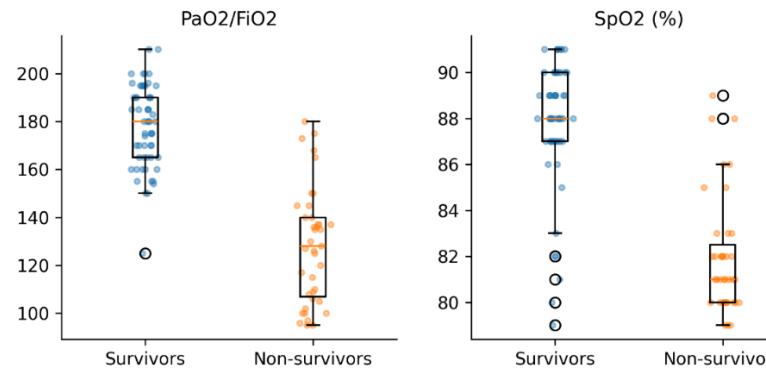


Figure 2.

Figure 3. Distribution of predicted mortality probability based on the combined model. The predicted probability of death calculated using the combined model was higher among non-survivors, and this distribution is shown in Figure 3.

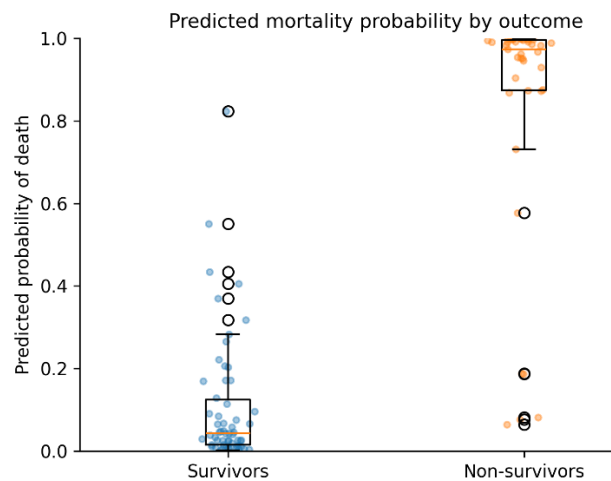


Figure 3.

#### 4. Discussion

The results of this study showed that baseline oxygenation parameters and systemic inflammatory markers play an important role in predicting in-hospital mortality in patients treated in intensive care with a diagnosis of ARDS. In particular, low PaO<sub>2</sub>/FiO<sub>2</sub> ratio, decreased SpO<sub>2</sub> level, and elevated IL-6 parameter demonstrated a strong and statistically significant association with the risk of death. These results once again confirm that the pathophysiology of ARDS is closely related to both hypoxemia and hyperinflammatory response and highlight the importance of early-stage risk stratification in clinical practice.

The PaO<sub>2</sub>/FiO<sub>2</sub> ratio is one of the most widely used parameters for assessing the severity of ARDS and also provides important information about the prognosis of the disease. Previous studies have shown that low PaO<sub>2</sub>/FiO<sub>2</sub> reflects not only the degree of respiratory failure, but also systemic disease burden and the risk of multiorgan dysfunction, and consequently is associated with increased mortality [14,15]. Our results also support this concept and showed that PaO<sub>2</sub>/FiO<sub>2</sub> acts as an independent prognostic factor. In this regard, a low value of this parameter during initial assessment may serve as a basis for planning more aggressive and early interventions in clinical decision-making.

The role of SpO<sub>2</sub> is particularly noteworthy from a practical perspective, because this parameter is non-invasive, rapid, and widely accessible. Previous studies have shown that saturation-based indices such as SpO<sub>2</sub>/FiO<sub>2</sub> can be used as an alternative to arterial blood gas analyses and provide sufficiently high accuracy in predicting mortality [16]. In our study as well, low SpO<sub>2</sub> level was significantly associated with the risk of death, indicating that even simple monitoring parameters can have high clinical value when interpreted correctly. Especially in resource-limited settings, SpO<sub>2</sub>-based assessment may serve as an effective and practical method of risk stratification.

The role of inflammatory processes in ARDS has been widely investigated in recent years, and IL-6 is considered one of the central mediators of these processes. Elevated IL-6

level, one of the main components of the cytokine storm phenomenon, has been associated with severe clinical course, multiorgan failure, and high mortality [17,18]. Our results also confirmed previous data in this direction and showed that high IL-6 level is independently associated with an increased risk of death. This emphasizes the importance of IL-6 not only as a diagnostic but also as a prognostic marker and suggests that it may potentially play a role in the selection of targeted treatment strategies.

One of the important findings of this study is that the combined assessment of oxygenation parameters and inflammatory markers provides higher prognostic accuracy. Previous studies have shown that, compared with models based on a single biomarker, multicomponent models allow patients to be divided more accurately into risk groups and guide clinical decision-making more precisely [19]. The increase in AUC in our combined model also clearly demonstrated the superiority of this approach. This shows that in complex and heterogeneous syndromes such as ARDS, a multidimensional approach is more appropriate.

The heterogeneity of ARDS and the presence of different clinical phenotypes also play an important role in interpreting the results. Studies have shown that patients with a hyperinflammatory phenotype have both higher levels of inflammatory markers and a significantly increased risk of mortality [20]. In this regard, the assessment of biomarkers such as IL-6 may help determine not only the

current condition but also the phenotype to which the patient belongs, which is important for the application of personalized treatment approaches.

At the same time, mortality in ARDS is not limited only to oxygenation and inflammation, and other systemic factors also influence this process. Various studies have shown that high levels of parameters such as D-dimer, CRP, ferritin, and NLR are associated with poor clinical outcomes [21]. This once again shows that ARDS is a multifactorial pathological process and requires a complex approach for its prediction. In this context, the parameters selected in our study constitute an optimal balance in terms of both clinical accessibility and prognostic significance.

Another important point is the prognostic significance of changes in oxygenation parameters over time. Previous studies have shown that worsening of PaO<sub>2</sub>/FiO<sub>2</sub> and other oxygenation indices during the course of the disease is closely associated with mortality, and changes observed particularly in the first days may provide critical prognostic information [22]. This indicates that not only baseline parameters, but also their dynamic monitoring should be taken into account in clinical decision-making.

At the same time, the patient's age and comorbid conditions are also important determinants affecting outcomes. Previous studies have shown that increasing age and the presence of concomitant diseases significantly increase mortality risk [23].

Evaluation of these factors together with biomarkers allows the construction of more accurate and clinically useful prognostic models.

Some limitations of this study should be considered. Due to the retrospective design, completeness of data and selection bias cannot be excluded, and the single-center nature of the study may limit the generalizability of the results. In addition, evaluation of only baseline parameters does not allow reflection of the time-varying effects of biomarkers. In the future, conducting larger and prospective studies is important to confirm and expand these results.

Nevertheless, the main strength of the study is that it presents an effective and applicable prognostic approach based on parameters easily obtained in daily clinical practice. This approach may be particularly important in intensive care settings for early risk stratification, optimal allocation of resources, and selection of personalized treatment strategies.

## 5. Conclusion

This study showed that PaO<sub>2</sub>/FiO<sub>2</sub>, SpO<sub>2</sub>, and IL-6 parameters measured during hospitalization in ARDS patients have important prognostic significance in the assessment of in-hospital mortality. Low PaO<sub>2</sub>/FiO<sub>2</sub> and SpO<sub>2</sub> levels reflected more severe oxygenation impairment, while high IL-6 level reflected a stronger systemic

inflammatory response and was significantly associated with the risk of death.

Among individual parameters, PaO<sub>2</sub>/FiO<sub>2</sub> showed the highest prognostic performance; however, combining oxygenation parameters with IL-6 further increased the discrimination ability of the model. This result shows that mortality in ARDS is determined not only by hypoxemia, but also by the intensity of the systemic inflammatory response.

Thus, a combined approach based on PaO<sub>2</sub>/FiO<sub>2</sub>, SpO<sub>2</sub>, and IL-6 parameters may be a simple, accessible, and clinically useful tool for early risk stratification in ARDS patients. This model may help in the early identification of high-risk patients in intensive care, strengthening of monitoring, and individualization of treatment strategy. In the future, confirmation of these results through larger, multicenter, and prospective studies would be appropriate.

## Declarations

### Ethical approval and consent to participate

The study protocol was approved by the Ethics Committee of Baku Medical Plaza Medical Center (Protocol number: BMP-06-2025; approval date: 18 June 2025). The study was conducted in accordance with the principles of the Declaration of Helsinki. Due to the retrospective design, individual written informed consent was not obtained from patients, and all patient data were anonymized before analysis.

## Consent for publication

Not applicable.

## Availability of data and materials

The data used or analyzed during the current study are not publicly available due to institutional and patient confidentiality. However, they may be obtained from the corresponding author upon reasonable request, provided that ethical and institutional permission is obtained.

## Competing interests

The authors declare that they have no competing interests.

## Funding

No external financial support was received for this study.

## Authors' contributions

KG proposed the idea of the study, participated in its design, contributed to the interpretation of the results, and participated in the preparation of the manuscript. GM and AM participated in data collection and preparation of the manuscript. AA and VA contributed to clinical interpretation and performed critical revision of the manuscript. IB provided methodological supervision, participated in the interpretation of the results, and performed the final revision. All authors read and approved the final version of the manuscript.

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