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Original Article

Predictive Value in Assessment of Acute Respiratory Distress Syndrome (ARDS)

Hamed Mostafa Ouda^{1*}; Ahmad Ali Abu-Naglah²; Mokhles Abdelfadil Ibrahim Zineldin¹; Ibrahim Fathi¹

¹ Department of Chest Diseases, Damietta Faculty of Medicine, Al-Azhar University, Damietta, Egypt.

² Department of Chest Diseases, Damietta Faculty of Medicine, Al-Azhar University, Damietta, Egypt.

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ABSTRACT

Background: Pneumonia is a major cause of acute respiratory failure and mortality in critically ill patients. Early and accurate prediction of mortality risk is essential for guiding clinical decisions and optimizing outcomes. Several clinical scoring systems are available, including the Oxygenation Index (OI), Berlin definition, modified Murray score, and the American European Consensus Conference (AECC) definition, but their relative predictive performance in pneumonia-associated respiratory failure remains uncertain.

Patients and Methods: This prospective observational study included patients admitted with pneumonia-associated respiratory failure. Sociodemographic data, comorbidities, and risk factors were recorded. The predictive performance of four respiratory severity scores OI, Berlin definition, modified Murray score, and AECC definition were assessed on days 1 to 4 of admission. Receiver operating characteristic curves were generated, and area under the curve values with 95% confidence intervals were calculated to evaluate each score's ability to predict 28-day mortality.

Results: The study showed a balanced gender distribution, mean age of 45.3 years, and high comorbidity burden. On day 1, all scores performed poorly (AUCs ~0.5). From day 2 onward, OI demonstrated a marked and progressive increase in predictive accuracy (AUC: 0.790 on day 2; 0.881 on day 3; 0.985 on day 4), while the modified Murray score showed moderate improvement (AUC: 0.847 on day 4). In contrast, the Berlin and AECC definitions consistently demonstrated poor and declining predictive performance, with AUCs falling below 0.5. Overall, OI outperformed all other scoring systems across all time points.

Conclusion: The Oxygenation Index is a robust and dynamic predictor of 28-day mortality in pneumonia patients, showing superior temporal improvement compared to the Berlin and AECC definitions and the modified Murray score. Routine application of OI may enhance prognostication and guide timely interventions in pneumonia-associated respiratory failure.

Keywords: Pneumonia; Oxygenation Index; Berlin Definition; Modified Murray Score; AECC Definition



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* Corresponding author

Email: hamedmostafa1997@yahoo.com

INTRODUCTION

Acute respiratory distress syndrome (ARDS) is a life-threatening form of acute hypoxemic respiratory failure characterized by noncardiogenic pulmonary edema, reduced lung compliance, and severe impairment of gas exchange. Despite advances in supportive care, the syndrome continues to be associated with substantial morbidity and mortality, with recent estimates indicating overall mortality rates approaching 40%. Several evidence-based interventions have improved survival in selected ARDS populations, including low tidal volume ventilation, prone positioning, and supported by a single trial-early administration of neuromuscular blocking agents (NMBAs) ⁽¹⁾. Additionally, two randomized controlled trials (RCTs) have suggested that extracorporeal membrane oxygenation (ECMO) may confer a survival benefit in carefully selected patients with severe ARDS ⁽²⁾.

However, the impact of these therapeutic strategies is limited by delayed or missed recognition of ARDS. Studies indicate that up to two-thirds of patients who fulfill diagnostic criteria are not identified as having ARDS at the time of onset, leading to delayed initiation of protective ventilation strategies and escalation of care ⁽³⁾. This under-recognition is partly attributed to the limitations of current consensus definitions, which demonstrate low sensitivity in routine clinical practice ⁽⁴⁾.

ARDS remains a syndromic diagnosis lacking a definitive biomarker or diagnostic test. Since its first description nearly six decades ago, several definitions have been proposed, including the American European Consensus Conference (AECC) criteria and, more recently, the Berlin definition ⁽⁵⁾. Yet even the Berlin criteria remain debated, as they rely predominantly on the ratio of arterial oxygen tension to inspired oxygen fraction ($\text{PaO}_2/\text{FiO}_2$) while neglecting other pathophysiological determinants such as lung compliance and mechanical properties, which strongly influence outcomes ⁽⁶⁾.

In response to these limitations, multiple adjunctive scoring systems have been developed to refine risk stratification. The Murray Lung Injury Score (LIS), for example, incorporates $\text{PaO}_2/\text{FiO}_2$, positive end-expiratory pressure (PEEP), lung compliance, and chest radiographic findings to quantify the severity of lung injury ⁽⁷⁾. Similarly, the oxygenation index (OI), calculated as $\text{mean airway pressure} \times \text{FiO}_2 \times 100 / \text{PaO}_2$, integrates the effect of ventilatory pressure and has shown superior prognostic performance compared to $\text{PaO}_2/\text{FiO}_2$ alone in several studies ⁽⁸⁾. Moreover, extravascular lung water index (EVLWI) has been proposed as a potential criterion for ARDS diagnosis and severity assessment ⁽⁹⁾.

Accurate, timely identification of ARDS severity and prognosis is essential for guiding the allocation and timing of advanced therapies such as prone positioning, NMBAs, and ECMO. Because these interventions carry substantial risks and resource demands, their optimized use is of considerable clinical and socioeconomic importance ⁽¹⁰⁾. Developing predictive tools that can reliably estimate mortality risk early in the disease course could therefore improve outcomes through more personalized therapeutic decision-making.

So, this study aimed to determine the most accurate early predictor and the optimal time point within the first four days after intubation for predicting 28-day mortality in patients with ARDS.

PATIENTS AND METHODS

Study Design and Population: This prospective observational study was conducted from July 2024 to May 2025 in the intensive care units (ICUs) of Al-Azhar University Hospital in Damietta, Egypt. A total of 50 mechanically ventilated adult patients fulfilling the criteria for acute respiratory distress syndrome were enrolled. ARDS severity was evaluated daily during the first four days after endotracheal intubation using four different scoring systems: the oxygenation index (OI), the modified Murray score without radiological components (Murray_mod), and the AECC and Berlin definitions. The study was conducted in accordance with the Declaration of Helsinki ethical codes. Approval was obtained from the institutional ethics committee of the Faculty of Medicine, Al-Azhar University (Damietta branch).

Inclusion and Exclusion Criteria: Eligible participants were adult patients diagnosed with ARDS according to the Berlin definition at the time of ICU admission. Patients were excluded if they had clinical or echocardiographic evidence of cardiac decompensation, or if their diagnosis of ARDS was uncertain or confounded by other causes of respiratory failure. All participants were enrolled consecutively during the study period.

Data collection

Clinical and Laboratory Assessment: Upon enrollment, all patients underwent comprehensive assessment, including full medical history and thorough physical examination (general and local). Routine laboratory investigations were performed, comprising complete blood count, blood glucose, liver function tests, and serum creatinine. Cardiac evaluation included 12-lead electrocardiography (ECG) and transthoracic echocardiography to rule out cardiogenic pulmonary edema. Chest imaging consisted of chest radiography and computed tomography (CT) to support the diagnosis and exclude alternative causes of respiratory failure.

ARDS Severity Scoring: To assess disease severity, four established scoring systems were applied to all enrolled patients during the first four days after intubation: the oxygenation index (OI), the Berlin definition, the American European Consensus Conference (AECC) definition, and a modified Murray score excluding radiographic criteria.

The oxygenation index incorporates both oxygenation and ventilatory parameters and is calculated as $\text{mean airway pressure} \times \text{FiO}_2 \times 100 / \text{PaO}_2$. By integrating the effect of ventilatory pressures on oxygenation, the OI provides a more comprehensive estimate of gas exchange impairment than the $\text{PaO}_2/\text{FiO}_2$ ratio alone. Several studies have demonstrated its superior prognostic value in predicting outcomes among ARDS patients ⁽¹¹⁾.

The Berlin definition, proposed in 2012, stratifies ARDS severity into mild, moderate, and severe categories based solely on $\text{PaO}_2/\text{FiO}_2$ thresholds while receiving a minimum positive end-expiratory pressure (PEEP) of 5 cmH₂O. This definition also requires bilateral pulmonary infiltrates on imaging and the absence of left atrial hypertension as the primary cause of edema ⁽¹²⁾. Although widely used, it does not account for pulmonary compliance or ventilatory mechanics, which are known to influence outcomes.

The earlier AECC definition similarly classifies ARDS severity according to $\text{PaO}_2/\text{FiO}_2$ thresholds, but without standardized PEEP requirements or time frames, which has contributed to variability in its application ⁽¹³⁾. While historically important, the AECC criteria are now considered less precise than the Berlin definition yet was included in this study for comparative evaluation.

The modified Murray score adapted from the original Murray Lung Injury Score—was used to incorporate key physiological markers while excluding radiographic assessment, which has been criticized for poor reproducibility. This version includes $\text{PaO}_2/\text{FiO}_2$, PEEP, and static lung compliance, providing a composite measure of lung injury severity ⁽¹⁴⁾.

Outcomes: The *primary* outcome of the study was 28-day all-cause mortality among patients diagnosed with ARDS and requiring invasive mechanical ventilation. Mortality status was determined from ICU records and confirmed through hospital documentation at 28 days following intubation. *Secondary* outcomes included the daily trajectory of ARDS severity scores (OI, Berlin definition, AECC definition, and modified Murray score) during the first four days after intubation, allowing assessment of their temporal evolution and predictive trends.

Statistical Analysis: All data were collected prospectively and analyzed using standard statistical software. Continuous variables were expressed as mean \pm standard deviation or median with

interquartile range as appropriate, and categorical variables as counts and percentages. To evaluate the prognostic performance of each severity index, receiver operating characteristic (ROC) curve analysis was performed, plotting sensitivity versus 1–specificity at various thresholds. The area under the ROC curve (AUC) was calculated to quantify the discriminative ability of each score for predicting 28-day mortality. Comparisons between AUCs were conducted to determine which index had superior predictive accuracy. Statistical significance was defined as a two-sided p value <0.05.

RESULTS

The study enrolled 50 patients with confirmed ARDS who required invasive mechanical ventilation. The cohort demonstrated a nearly balanced gender distribution (56% male and 44% female) with a mean age of 45.3 ± 17.9 years. More than half of the participants were married (52%), followed by single (26%), widowed (16%), and divorced (6%) individuals. Regarding place of residence, 66% of patients were from rural areas and 34% from urban areas (**Table 1**).

All patients (100%) had pneumonia as a precipitating factor for ARDS. Additional comorbidities included smoking in 36% of patients, diabetes mellitus in 26%, and drowning-related lung injury in 24%. This distribution highlights the heterogeneous risk profile within the studied cohort (**Table 2**).

The prognostic performance of four ARDS severity scoring indices, the Oxygenation Index, the Berlin definition, the modified Murray score (Murray_mod), and the AECC definition were assessed across the first four days following intubation. On day 1, all four scores demonstrated poor discriminatory ability, with AUC values approximating 0.5, indicating performance no better than chance (OI: 0.492; Berlin: 0.462; Murray_mod: 0.484; AECC: 0.433; $p > 0.05$ for all). By day 2, a marked divergence became evident. OI showed significant improvement with an AUC of 0.790 ($p < 0.0001$), indicating good discrimination, while the Berlin (0.415), Murray_mod (0.530), and AECC (0.415) scores remained low and non-significant. This trend continued on day 3, where OI (0.881; $p < 0.0001$) and Murray_mod (0.772) demonstrated strong predictive performance, whereas Berlin and AECC dropped to 0.202 each, suggesting poor and potentially misleading prognostic utility. On day 4, OI achieved near-perfect discrimination (0.985; $p < 0.0001$), and Murray_mod also performed well (0.847), while Berlin and AECC further declined to 0.08 each. Overall, the mean AUC across all four days was highest for OI (0.787), followed by Murray_mod (0.658), while Berlin and AECC consistently underperformed (0.290 and 0.283, respectively) (**Table 3**).

ROC curves were constructed using individual patient scores

from each model (OI, Berlin, AECC, Murray_mod) plotted against 28-day mortality status. For each possible threshold, sensitivity and specificity were calculated, and AUC values were used to quantify overall discriminative performance. On day 1, all scores produced ROC curves close to the diagonal line (no discrimination). By day 2, the ROC curve for OI bowed markedly toward the upper left corner, demonstrating better sensitivity at lower false positive rates, while the other scores remained near the diagonal. On day 3, the ROC curves for OI and Murray_mod became strongly convex, indicating robust predictive power, while Berlin and AECC

showed diminished curvature. By day 4, OI achieved an almost perfect ROC curve shape, while Berlin and AECC collapsed to nearly flat curves at the bottom, confirming their lack of clinical utility (**Figures 1–4**).

When comparing the overall discriminative ability across time points, the best mean ROC-AUC for predicting 28-day mortality was observed on day 2 (mean AUC = 0.538), followed by day 3 (0.514), whereas the mean ROC-AUCs were below 0.5 on day 1 and day 4 (**Table 4**).

Table (1): Sociodemographic characteristic data of the study population.

Variable	Number of patients	
Gender	Male	28(56%)
	Female	22(44%)
Age	Mean±SD	45.32±17.92
Marital status	Married	26(52%)
	Single	13(26%)
	Widowed	8(16%)
	Divorced	3(6%)
Residency	Rural	33(66%)
	Urban	17(34%)

Table (2): Different Comorbidities in study population.

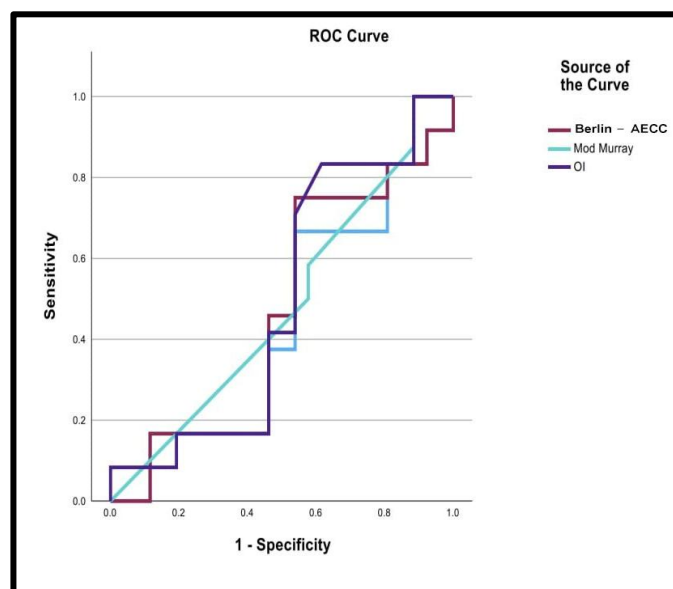
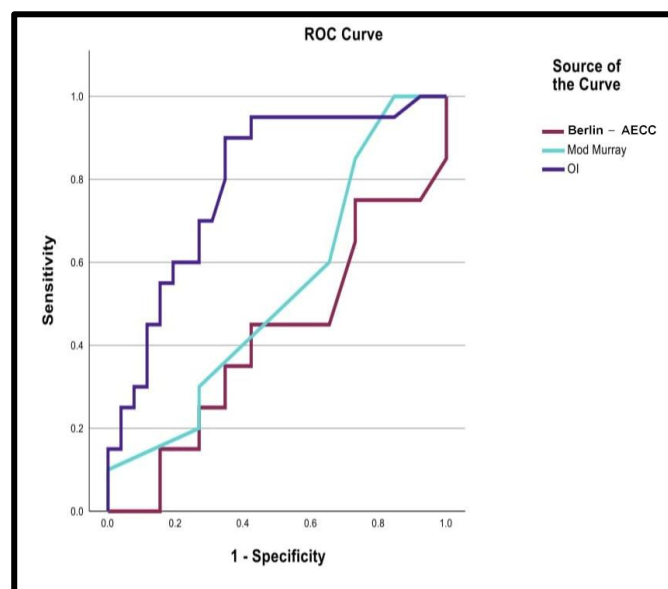
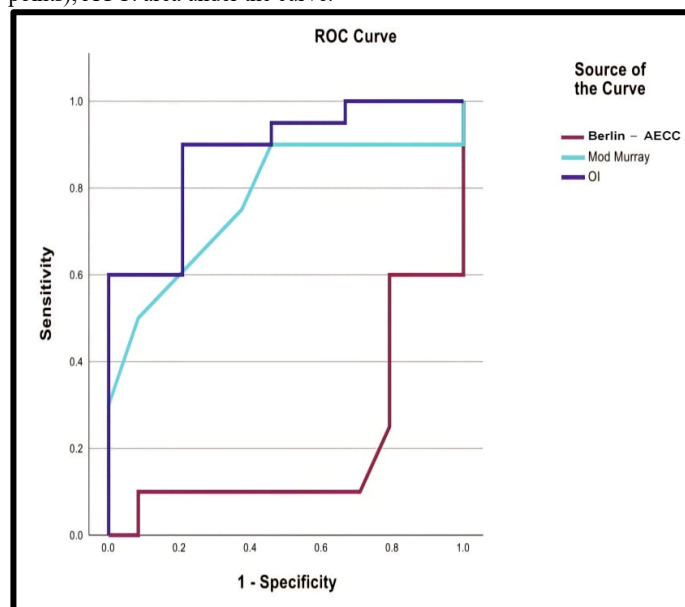
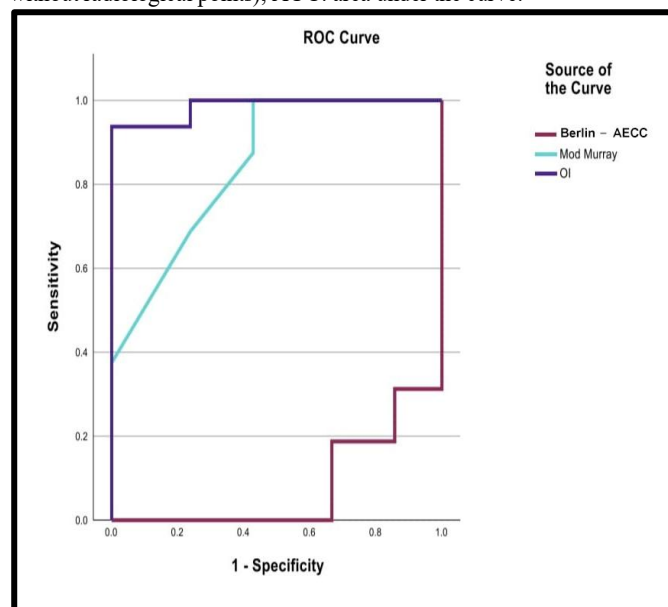
Variable	Number	Percentage	Variable	Number	Percentage
Smoking	18	36%	HF	3	6%
Addiction	7	14%	Arrhythmia	4	8%
COPD	8	16%	CLD	6	12%
BA	8	16%	CKD	8	16%
Bronchiectasis	3	6%	SLE	4	8%
TB	3	6%	RA	2	4%
OSA/OHS	5	10%	Stroke	7	14%
DM	13	26%	Drowning	12	24%
HTN	10	20%	Trauma	11	22%
IHD	2	4%	Pneumonia	50	100%

Table (3): Prediction of 28-days-mortality by OI, Berlin-, AECC-definition and modified Murray-score in first 4 days: All patients.

Variable		OI	Berlin	Mod-Murray	AECC
Day1	AUC	0.492	0.462	0.484	0.433
	95% CI	0.324-0.660	0.296-0.627	0.322-0.646	0.270-0.595
	P-value	0.925	0.649	0.846	0.418
AUC-Day2	AUC	0.79	0.415	0.53	0.415
	95% CI	0.657-0.923	0.246-0.585	0.360-0.699	0.246-0.585
	P-value	<0.0001	0.327	0.730	0.327
AUC-Day3	AUC	0.881	0.202	0.772	0.202
	95% CI	0.781-0.981	0.059-0.345	0.623-0.921	0.059-0.345
	P-value	<0.0001	<0.0001	<0.0001	<0.0001
AUC-Day4	AUC	0.985	0.08	0.847	0.08
	95% CI	0.953-0.1018	0.004-0.165	0.726-0.967	0.004-0.165
	P-value	<0.0001	<0.0001	<0.0001	<0.0001
Mean AUC		0.787	0.28975	0.65825	0.2825

Table (4): Prediction of 28-days-mortality by OI, Berlin-, AECC-definition and modified Murray-score in Over four days: All patients, determination of best day.

Predictor	Day 1	Day 2	Day3	Day4
	AUC	AUC	AUC	AUC
OI	0.492	0.790	0.881	0.985
Berlin	0.462	0.415	0.202	0.080
Murray_mod	0.484	0.530	0.772	0.847
AECC	0.433	0.415	0.202	0.080
Mean AUC	0.46775	0.5375	0.514	0.498

**Figure (1):** ROC-AUC regarding 28 day-mortality (all patients; day 1). OI: oxygenation index; AECC: American European Consensus Conference; Murray_mod: modified Murray-score (sum of points without radiological points); AUC: area under the curve.**Figure (2):** ROC-AUC regarding 28 day-mortality (all patients; day 2). OI: oxygenation index; AECC: American European Consensus Conference; Murray_mod: modified Murray-score (sum of points without radiological points); AUC: area under the curve.**Figure (3):** ROC-AUC regarding 28 day-mortality (all patients; day 3). OI: oxygenation index; AECC: American European Consensus Conference; Murray_mod: modified Murray-score (sum of points without radiological points); AUC: area under the curve.**Figure (4):** ROC-AUC regarding 28d-mortality (all patients; day 4). OI: oxygenation index; AECC: American European Consensus Conference; Murray_mod: modified Murray-score (sum of points without radiological points); AUC: area under the curve.

DISCUSSION

The present study offers meaningful insights into the prognostic performance of various clinical scoring systems in predicting 28-day mortality among pneumonia patients, with particular emphasis on comparisons to established evidence from ARDS and pneumonia-related research. A key finding is the robust predictive capacity of the Oxygenation Index, which demonstrated a progressive and significant improvement in discriminative ability over time, from an AUC of 0.492 on Day 1 to 0.985 by Day 4. This temporal enhancement highlights the dynamic value of OI, underscoring its increasing reliability as patients' clinical status evolves.

Comparable results have been reported in prior investigations. **Rsovac *et al.*** ⁽¹⁵⁾ demonstrated that Day 3 OI provided markedly higher predictive accuracy for mortality compared to Day 1. Similarly, **Huber *et al.*** ⁽¹⁶⁾ observed that OI during the first two days of mechanical ventilation was the most reliable predictor of 28-day mortality. **Mamun *et al.*** ⁽¹⁷⁾ further showed that an OI ≥ 16.01 cm H₂O substantially elevated mortality risk, achieving high sensitivity (88.06%) and specificity (87.27%) even on Day 1. In COVID-19 ARDS cohorts, **Singh *et al.*** ⁽¹⁸⁾ reported that Day 1 OI yielded an AUC of 0.752 for mortality prediction, supporting its early utility. Collectively, these findings reinforce the current study's observation that OI consistently serves as a strong prognostic marker, with predictive accuracy that frequently strengthens over time.

Importantly, the current results also corroborate literature suggesting the superiority of OI over the PaO₂/FiO₂ ratio alone. Several studies have highlighted OI's enhanced prognostic accuracy, attributable to its incorporation of mean airway pressure, which reflects both ventilatory intensity and mechanical lung stress—factors not captured by PaO₂/FiO₂ ^(15,19). In contrast, the PaO₂/FiO₂ ratio, though widely utilized, has demonstrated only limited prognostic association with mortality in ARDS when considered in isolation. Thus, composite indices such as OI, which integrate both oxygenation and ventilatory parameters, provide more comprehensive and clinically relevant risk stratification ⁽¹⁹⁾.

Conversely, the present study found that the Berlin definition exhibited consistently poor discriminatory ability for 28-day mortality (AUC 0.462 on Day 1 declining to 0.08 on Day 4). While the Berlin definition remains a widely accepted framework for diagnosing ARDS and classifying severity based on hypoxemia, its role as a standalone prognostic tool appears limited in this pneumonia-specific cohort. Similar limitations have been raised in prior studies, which reported only marginal predictive value for Berlin staging, with AUCs often around 0.60.

Zhang *et al.* ⁽²⁰⁾ also noted a lack of consistent correlation between Berlin-defined severity and mortality outcomes. In burn-related ARDS, **Bordes and Cancio** ⁽²¹⁾ reported only moderate predictive value (AUROC 0.69). Although the Berlin definition improved upon the original AECC definition by standardizing PEEP thresholds and refining radiographic criteria, it has been criticized for overreliance on PaO₂/FiO₂ ratios, lack of dynamic adaptability, and omission of variables such as airway pressures or etiology all of which carry prognostic relevance ^(19,23). Furthermore, its moderate diagnostic sensitivity (89%) and low specificity (63%) against autopsy findings further constrain its predictive utility ⁽²²⁾. The declining AUCs observed in the present analysis, particularly values below 0.5, raise concerns that Berlin criteria may even yield misleading prognostic inferences in this population.

The modified Murray score, while not outperforming OI, demonstrated gradually increasing predictive value, achieving an AUC of 0.847 on Day 4. This suggests that, although less sensitive to early disease changes, the Murray score becomes more reliable as illness progresses. The Murray or Lung Injury Score has been widely applied in stratifying acute lung injury severity and guiding ECMO selection, as it incorporates multiple dimensions including radiographic infiltrates, PaO₂/FiO₂, PEEP, and compliance ⁽²³⁾. Nonetheless, reported predictive performances have varied.

Schwaiger ⁽²⁴⁾ noted suboptimal discrimination (AUC <0.6) in the first two days, in contrast with the present findings of improvement by Day 3 and Day 4. Differences may reflect variations in patient populations, methodology, or score modifications. Notably, Murray scores ≥ 3 –4, especially with PaO₂/FiO₂ <100 on FiO₂ >90%, have consistently been associated with mortality rates exceeding 80% and the need for rescue therapies such as ECMO ⁽²⁵⁾.

Finally, the poor performance of the AECC definition in the current study, with AUCs approximating random chance, reflects longstanding criticisms of its limited prognostic accuracy. Established in 1994, AECC criteria were the first internationally standardized definition for ARDS and acute lung injury yet were criticized for low specificity (51% versus autopsy) and variable interobserver reliability for radiographic criteria. Its reliance on non-standardized ventilatory support (e.g., absence of mandatory PEEP) and static hypoxemia thresholds often resulted in inconsistent patient classification ⁽²⁶⁾.

Although early studies noted associations between oxygenation impairment at 24 hours and outcome, the AECC definition's inability to dynamically account for ventilatory settings or evolving physiology constrained its clinical utility. The current findings further reinforce these limitations, underscoring its inadequacy as a prognostic tool in contemporary practice.

Conclusion: The study underscores the importance of using dynamic, physiology-based indices for prognostication in pneumonia-associated respiratory failure. Incorporating tools such as the Oxygenation Index into routine practice may enable more accurate risk stratification and support timely, targeted interventions, ultimately improving critical care outcomes.

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