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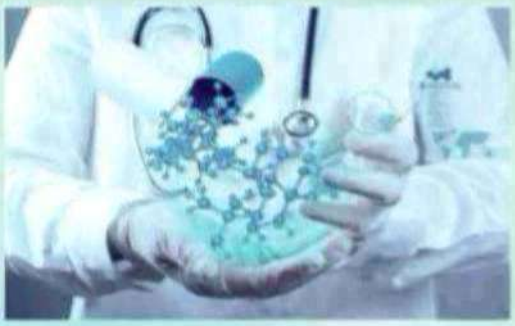

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ACUTE HYPOXEMIC RESPIRATORY FAILURE IN THE ICU: PREDICTORS OF PROLONGED MECHANICAL VENTILATION AND 30-DAY MORTALITY

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✓ ***Resume***

Acute hypoxemic respiratory failure (AHRF) is one of the most frequent indications for admission to the intensive care unit (ICU) and a leading cause of ICU mortality worldwide. Mechanical ventilation (MV) remains the cornerstone of respiratory support in AHRF; however, prolonged ventilation is independently associated with ventilator-induced lung injury, ventilator-associated pneumonia, diaphragmatic dysfunction, and increased mortality. The identification of early predictors of prolonged MV and 30-day mortality in AHRF patients is therefore of critical clinical importance, particularly in Central Asian ICUs where evidence-based risk stratification tools derived from local populations are lacking.

Keywords: acute hypoxemic respiratory failure, mechanical ventilation, ARDS, PaO_2/ $PaCO_2$ ratio, ventilator-associated pneumonia, lung-protective ventilation, intensive care unit, 30-day mortality, weaning.

O'TKIR GIPOKSEMIK NAFAS YETISHMOVCHILIGI REANIMATOLOGIYA BO'LIMIDA: SUN'IY O'PKA VENTILYATSIYASI DAVOMIYLIGINI VA 30 KUNLIK O'LIM KO'RSATKICHINI BASHORAT QILUVCHI ERTA OMILLAR

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✓ ***Rezyume***

Dolzarbligi. O'tkir gipoksemik nafas yetishmovchiligi (OGNY) reanimatologiya bo'limiga yotqizishning eng ko'p uchraydigan sabablaridan biri bo'lib, butun dunyo bo'ylab reanimatologiya bo'limlarida o'lim ko'rsatkichining asosiy omili hisoblanadi. Sun'iy o'pka ventilyatsiyasi (SOV) OGNY da nafas qo'llab-quvvatlashning asosiy usuli bo'lib qolmoqda; biroq uzoq muddatli ventilyatsiya ventilyator bilan bog'liq o'pka shikastlanishi, ventilyator bilan bog'liq pnevmoniya, diafragma disfunktsiyasi va o'lim ko'rsatkichining ortishi bilan mustaqil ravishda bog'liqdir. OGNY bemorlarida uzoq muddatli SOV va 30 kunlik o'lim ko'rsatkichining erta bashoratchilarini aniqlash katta klinik ahamiyatga ega, ayniqsa mahalliy aholidan olingan dalillarga asoslangan xavfni stratifikatsiya qilish vositalari mavjud bo'lmagan Markaziy Osiyo reanimatologiya bo'limlarida.

Kalit so'zlar: o'tkir gipoksemik nafas yetishmovchiligi, sun'iy o'pka ventilyatsiyasi, o'tkir respiratory distress-sindrom, $PaO_2/PaCO_2$ nisbati, ventilyator bilan bog'liq pnevmoniya, o'pkani himoya qiluvchi ventilyatsiya, reanimatologiya bo'limi, 30 kunlik o'lim, veyning.

ОСТРАЯ ГИПОКСЕМИЧЕСКАЯ ДЫХАТЕЛЬНАЯ НЕДОСТАТОЧНОСТЬ В ОРИТ: РАННИЕ ПРЕДИКТОРЫ ПРОДЛЁННОЙ ИВЛ И 30-ДНЕВНОЙ ЛЕТАЛЬНОСТИ

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✓ ***Резюме***

Острая гипоксемическая дыхательная недостаточность (ОГДН) является одним из наиболее частых показаний для госпитализации в отделение реанимации и интенсивной терапии (ОРИТ) и ведущей причиной летальности в ОРИТ во всём мире. Искусственная вентиляция лёгких (ИВЛ) остаётся краеугольным камнем респираторной поддержки при ОГДН; однако пролонгированная вентиляция независимо ассоциирована с вентилятор-индуцированным повреждением лёгких, вентилятор-ассоциированной пневмонией, дисфункцией диафрагмы и повышением летальности. Ранняя идентификация пациентов с ОГДН, подверженных риску длительной зависимости от респиратора и летального исхода, имеет критическое клиническое значение — особенно в реанимационных отделениях стран Центральной Азии, где доказательные инструменты стратификации риска на основе местных популяций в настоящее время отсутствуют.

Ключевые слова: острая гипоксемическая дыхательная недостаточность, искусственная вентиляция лёгких, острый респираторный дистресс-синдром, индекс $PaO_2/PaCO_2$, вентилятор-ассоциированная пневмония, протективная вентиляция лёгких, ОРИТ, 30-дневная летальность, вейнинг.

Relevance

Acute hypoxemic respiratory failure (AHRF), defined as a $PaO_2/PaCO_2$ ratio below 300 mmHg with an acute onset requiring supplemental oxygen or ventilatory support, represents one of the most common and life-threatening conditions encountered in the ICU.[1] At its most severe end, AHRF manifests as acute respiratory distress syndrome (ARDS), a diffuse inflammatory lung injury characterized by bilateral pulmonary infiltrates, severe hypoxemia ($PaO_2/PaCO_2$ <100–200 mmHg), and reduced respiratory system compliance.[2] The Berlin Definition of ARDS, published in 2012, stratified severity into mild ($PaO_2/PaCO_2$ 200–300 mmHg), moderate (100–200 mmHg), and severe (<100 mmHg) categories, providing a widely adopted clinical framework for diagnosis and outcome prediction.[2]

Globally, ARDS affects an estimated 3 million patients annually, accounting for approximately 10% of all ICU admissions and 23% of all mechanically ventilated patients.[3] Despite decades of research and the adoption of lung-protective ventilation strategies — including low tidal volume (VT ≤6 mL/kg of predicted body weight), limitation of plateau pressure (Pplat ≤30 cmH_2O), and individualized PEEP titration — ICU mortality in moderate-to-severe ARDS remains 30–45%.[3,4] Prolonged mechanical ventilation, defined as MV duration exceeding 7 days, is independently associated with increased morbidity and mortality.[5]

Early identification of AHRF patients at risk for prolonged ventilator dependence and fatal outcome is essential for timely initiation of advanced rescue therapies — including prone positioning, neuromuscular blockade, and extracorporeal membrane oxygenation (ECMO) — and for informed communication with patients' families.[4,6] Current risk stratification relies primarily on the $PaO_2/PaCO_2$ ratio and SOFA score; however, emerging evidence suggests that dynamic parameters such as driving pressure ($\Delta P = Pplat - PEEP$) and mechanical power offer superior predictive value.[7]

The objective of this study was to prospectively identify early predictors of prolonged mechanical ventilation (>7 days) and 30-day ICU mortality in patients with acute hypoxemic respiratory failure, and to evaluate the discriminatory performance of a combined multiparameter model in comparison with the $PaO_2/PaCO_2$ ratio and SOFA score used individually.

Materials and methods

Study design and patient selection

A prospective observational study was conducted in the ICU of the Republican Specialized Scientific-Practical Medical Center of Pulmonology (Tashkent, Uzbekistan) from February 2021 to February 2024. The study protocol was approved by the Institutional Ethics Committee (Protocol No. 6, dated 01.02.2021). Written informed consent was obtained from patients or their legal representatives prior to enrollment.

Inclusion criteria: age ≥18 years; AHRF defined as $PaO_2/PaCO_2$ <300 mmHg with acute onset (<1 week); requirement for invasive mechanical ventilation within 24 hours of ICU admission; bilateral

pulmonary infiltrates on chest radiograph or CT not fully explained by cardiac failure or fluid overload.[2] Exclusion criteria: age <18 years; MV initiated >24 hours before ICU admission; established chronic respiratory failure requiring home ventilatory support; do-not-intubate order; ICU stay <48 hours; pregnancy; transfer from another ICU with MV duration >48 hours.

Ventilatory management

All patients were ventilated according to a standardized lung-protective protocol: VT 6 mL/kg predicted body weight, Pplat ≤30 cmH_2O, PEEP titrated by the ARDSNet low-PEEP/$PaCO_2$ table targeting SpO_2 88–95%.[4] Driving pressure was calculated as ΔP = Pplat − PEEP and recorded at 0, 24, and 72 hours. Prone positioning was applied for ≥16 hours/day in patients with $PaO_2/PaCO_2$ <150 mmHg and $PaCO_2$ ≥0.6 after ≥12 hours of optimized conventional ventilation. Weaning was initiated when the patient met predefined readiness criteria: $PaCO_2$ ≤0.4, PEEP ≤8 cmH_2O, hemodynamic stability, adequate spontaneous respiratory effort, and GCS ≥10.

Data collection and laboratory investigations

The following variables were recorded at ICU admission (Hour 0) and at 24 and 72 hours: $PaO_2/PaCO_2$ ratio, static respiratory system compliance (Crs = VT / [Pplat − PEEP]), driving pressure (ΔP), SOFA score, arterial lactate, serum albumin, CRP, PCT, WBC, serum creatinine, bilirubin, and platelet count. Etiology of AHRF and presence of immunosuppression were documented at admission.

Endpoints and definitions

The co-primary endpoints were: (1) prolonged MV defined as MV duration >7 days; and (2) 30-day all-cause ICU mortality. Secondary endpoints included ICU length of stay, incidence of VAP (CDC 2015 criteria), and successful extubation rate. Ventilator-free days (VFDs) at day 28 were calculated as 28 minus MV days for survivors; non-survivors received VFD = 0.

Statistical analysis

Statistical analyses were performed using SPSS Statistics 27.0 (IBM Corp.) and R 4.3.0. Continuous variables are expressed as median [Q1; Q3] or mean ± SD. Variables with $p<0.10$ in univariable logistic regression were entered into the multivariable model. Discriminatory performance was assessed by AUC-ROC. Statistical significance was defined as $p<0.05$.

Result and discussions

Baseline characteristics and outcomes

A total of 198 patients with AHRF requiring invasive MV were enrolled. Median age was 56 [44; 66] years; 124 patients (62.6%) were male.

Table 1. Baseline characteristics stratified by MV duration (n=198)

Parameter	MV ≤7 days (n=102)	MV >7 days (n=96)	p-value
Age, years	52 [40; 62]	60 [48; 70]	0.003
Male sex, n (%)	66 (64.7%)	58 (60.4%)	0.537
$PaO_2/PaCO_2$ (Hour 0), mmHg	198 [152; 248]	128 [88; 168]	<0.001
Crs (Hour 0), mL/cmH_2O	38.4 [28.6; 48.2]	24.8 [18.4; 32.6]	<0.001
Driving pressure ΔP, cmH_2O	11.2 [8.4; 14.6]	16.8 [13.2; 21.4]	<0.001
SOFA score (Day 0)	7 [5; 9]	11 [8; 13]	<0.001
Serum albumin, g/L	30.2 [26.4; 34.8]	22.4 [18.2; 26.8]	<0.001
PCT, ng/mL	8.4 [2.8; 22.4]	28.6 [12.4; 68.4]	<0.001
VAP during ICU stay, n (%)	12 (11.8%)	40 (41.7%)	<0.001
30-day mortality, n (%)	18 (17.6%)	58 (60.4%)	<0.001
VFDs at day 28, days	18 [12; 24]	0 [0; 6]	<0.001

Crs — static respiratory system compliance; ΔP — driving pressure; SOFA — Sequential Organ Failure Assessment; PCT — procalcitonin; VAP — ventilator-associated pneumonia; VFDs — ventilator-free days.

The most frequent etiologies were community-acquired pneumonia (82, 41.4%), sepsis-associated AHRF (54, 27.3%), and aspiration pneumonitis (28, 14.1%). ARDS was diagnosed in 148 patients (74.7%): mild in 38 (19.2%), moderate in 72 (36.4%), and severe in 38 (19.2%). Prolonged MV (>7 days) occurred in 96 patients (48.5%). The 30-day ICU mortality was 38.4% (76 patients). VAP was diagnosed in 52 patients (26.3%). Baseline characteristics are presented in Table 1.

Independent predictors of prolonged MV and 30-day mortality

Multivariable logistic regression identified four independent predictors (Table 2). The combined model achieved AUC = 0.87 (95% CI 0.82–0.92) for prolonged MV and AUC = 0.86 (95% CI 0.80–0.91) for 30-day mortality — superior to $PaO_2/PaCO_2$ alone (AUC 0.76; p=0.009) and SOFA alone (AUC 0.74; p=0.006).

Table 2. Independent predictors of prolonged MV (multivariable logistic regression)

Predictor	OR	95% CI	p-value
$PaO_2/PaCO_2$ <150 mmHg at Hour 0	4.18	2.14–8.16	<0.001
Driving pressure ΔP ≥15 cmH_2O	3.52	1.82–6.82	<0.001
SOFA score ≥10 at Day 0	2.94	1.54–5.62	0.001
Serum albumin <25 g/L	2.48	1.30–4.72	0.006

OR — odds ratio; CI — confidence interval; ΔP — driving pressure; SOFA — Sequential Organ Failure Assessment.

Discussion

This prospective study identified four early predictors of prolonged MV and 30-day ICU mortality in patients with AHRF: $PaO_2/PaCO_2$ <150 mmHg, driving pressure ≥15 cmH_2O, SOFA score ≥10, and serum albumin <25 g/L. The combined model demonstrated excellent discriminatory capacity (AUC = 0.87), substantially exceeding the performance of oxygenation index and SOFA score used in isolation.[3,7]

The predominance of $PaO_2/PaCO_2$ <150 mmHg as the strongest predictor (OR 4.18) is consistent with the Berlin ARDS stratification, in which moderate and severe categories carry progressively higher hospital mortality.[2] Serial oxygenation assessment in the first 24 hours of ventilation — a dynamic rather than static parameter — has been shown to be an even stronger predictor of outcome than the admission value alone, and is strongly recommended in routine practice.[3,8]

Driving pressure ≥15 cmH_2O (OR 3.52) supports the landmark findings of Amato et al., whose analysis of 3,562 ARDS patients demonstrated that driving pressure was the ventilatory variable most strongly associated with mortality — more so than VT or PEEP individually.[7] ΔP reflects the ratio of VT to functional lung size and serves as a surrogate for strain on remaining aerated units. Titrating ventilation to minimize ΔP rather than adhering to fixed VT targets represents a superior lung-protection strategy increasingly supported by physiological studies and clinical guidelines.[4,7]

SOFA score ≥10 (OR 2.94) reflects the critical role of extrapulmonary organ dysfunction in ventilator dependence. In AHRF, coexisting hemodynamic instability, acute kidney injury, hepatic dysfunction, and thrombocytopenia impair tissue oxygen utilization and delay respiratory recovery.[6] Hypoalbuminemia (<25 g/L; OR 2.48) reflects both nutritional depletion and acute-phase protein redistribution, contributing to pulmonary edema, diaphragmatic muscle wasting, and prolonged weaning — mechanisms also associated with the significantly higher VAP rate observed in the prolonged-MV group (41.7% vs. 11.8%; p<0.001).[9,10]

Limitations include the single-center design, incomplete microbiological speciation in 32% of patients, and potential confounding from corticosteroid use in a subgroup. Multicenter validation is required before the proposed model can be recommended for routine clinical implementation.

Conclusion

In patients with acute hypoxemic respiratory failure requiring invasive mechanical ventilation, four early predictors of prolonged MV and 30-day ICU mortality were identified: $PaO_2/PaCO_2$ <150 mmHg, driving pressure ≥15 cmH_2O, SOFA score ≥10, and serum albumin <25 g/L. The combined model achieved AUC = 0.87, substantially exceeding individual scoring systems. Routine assessment of these four parameters within the first 24 hours of ICU admission is recommended to identify high-risk patients requiring early escalation to advanced rescue strategies and targeted nutritional support.

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