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# IMPORTANCE OF DETERMINING RISK STRATIFICATION IN PATIENTS WITH PULMONARY ARTERIAL HYPERTENSION: A PROGNOSTIC AND THERAPEUTIC ANALYSIS

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**Abstract:** Pulmonary Arterial Hypertension (PAH) is a progressive and fatal disease characterized by increased pulmonary vascular resistance and right heart failure. The modern management of PAH relies heavily on a goal-oriented treatment strategy driven by regular risk assessment. This article presents a prospective clinical study conducted at the Department of Faculty Therapy of Andijan State Medical Institute. Using the IMRAD framework, the research evaluates the prognostic value of the multiparametric risk stratification strategy recommended by ESC/ERS guidelines in 54 patients with idiopathic and connective tissue disease-associated PAH. The study correlates risk strata (low, intermediate, high) with clinical outcomes and novel metabolic markers. The results demonstrate that patients maintaining a low-risk profile exhibit significantly better survival and functional capacity, while intermediate and high-risk status is associated with metabolic derangement and frequent hospitalization. The study concludes that rigorous, dynamic risk stratification is the cornerstone of effective PAH management in the local population.

**Keywords:** pulmonary arterial hypertension, risk stratification, right heart failure, prognosis, multiparametric assessment, metabolic markers.

# ЗНАЧЕНИЕ ОПРЕДЕЛЕНИЯ СТРАТИФИКАЦИИ РИСКА У ПАЦИЕНТОВ С ЛЕГОЧНОЙ АРТЕРИАЛЬНОЙ ГИПЕРТЕНЗИЕЙ: ПРОГНОСТИЧЕСКИЙ И ТЕРАПЕВТИЧЕСКИЙ АНАЛИЗ

**Аннотация:** Легочная артериальная гипертензия (ЛАГ) — это прогрессирующее и фатальное заболевание, характеризующееся повышением легочного сосудистого сопротивления и правожелудочковой недостаточностью. Современное ведение ЛАГ в значительной степени опирается на целевую стратегию лечения, определяемую регулярной оценкой риска. В данной статье представлено проспективное клиническое исследование, проведенное на кафедре факультетской терапии Андижанского государственного медицинского института. Используя структуру IMRAD, исследование оценивает прогностическую ценность мультипараметрической стратегии стратификации риска, рекомендованной руководствами ESC/ERS, у 54 пациентов с идиопатической ЛАГ и ЛАГ, ассоциированной с заболеваниями соединительной ткани. Исследование коррелирует страты риска (низкий, промежуточный, высокий) с клиническими исходами и новыми метаболическими маркерами. Результаты показывают, что пациенты, поддерживающие профиль низкого риска, демонстрируют значительно лучшую выживаемость и функциональную способность, в то время как промежуточный и высокий риск ассоциированы с метаболическими нарушениями и частой госпитализацией. Исследование делает вывод, что строгая динамическая стратификация риска является краеугольным камнем эффективного ведения ЛАГ в местной популяции.

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**Ключевые слова:** легочная артериальная гипертензия, стратификация риска, правожелудочковая недостаточность, прогноз, мультипараметрическая оценка, метаболические маркеры.

## O‘PKA ARTERIAL GIPERTENZIYASI BO‘LGAN BEMORLARDA XAVF STRATIFIKATSIYASINI ANIQLASHNING AHAMIYATI: PROGNOSTIK VA TERAPEVTIK TAHLIL

**Annotatsiya:** O‘pka arterial gipertenziyasi (O‘AG) o‘pka tomirlari qarshiligining oshishi va o‘ng qorincha yetishmovchiligi bilan tavsiflanuvchi, zo‘rayib boruvchi va o‘limga olib keluvchi kasallikdir. O‘AGni zamonaviy boshqarish muntazam xavfni baholashga asoslangan maqsadli davolash strategiyasiga tayanadi. Ushbu maqolada Andijon davlat tibbiyot institutining Fakultet terapiyasi kafedrasida o‘tkazilgan prospektiv klinik tadqiqot natijalari keltirilgan. IMRAD tuzilmasiga asoslangan ushbu ish idiopatik va biriktiruvchi to‘qima kasalliklari bilan bog‘liq O‘AG bo‘lgan 54 nafar bemorda ESC/ERS tavsiyalari bo‘yicha ko‘p parametrli xavfni tabaqalash strategiyasining prognostik ahamiyatini baholaydi. Tadqiqot xavf guruhlarini (past, o‘rta, yuqori) klinik natijalar va yangi metabolik markerlar bilan o‘zaro bog‘laydi. Natijalar shuni ko‘rsatadiki, past xavf profilini saqlab qolgan bemorlarda yashab qolish va funksional imkoniyatlar sezilarli darajada yaxshiroq bo‘ladi, o‘rta va yuqori xavf maqomi esa metabolik buzilishlar va tez-tez kasalxonaga yotish bilan bog‘liq. Tadqiqot qat’iy va dinamik xavf tabaqalanishi mahalliy aholi orasida O‘AGni samarali boshqarishning asosi ekanligi haqida xulosa qiladi.

**Kalit so‘zlar:** o‘pka arterial gipertenziyasi, xavfni tabaqalash, o‘ng qorincha yetishmovchiligi, prognoz, ko‘p parametrli baholash, metabolik markerlar.

### INTRODUCTION

Pulmonary Arterial Hypertension (PAH) is a complex vascular disease defined by elevated pulmonary artery pressure in the absence of left heart disease or lung parenchymal disorders. The pathological hallmark involves remodeling of the small pulmonary arteries, leading to increased right ventricular (RV) afterload and ultimately, right heart failure. Historically, the prognosis for PAH was dismal; however, the advent of vasoactive therapies targeting the endothelin, nitric oxide, and prostacyclin pathways has improved survival. Despite these advances, mortality rates remain unacceptably high, primarily due to delayed treatment escalation.

Current international guidelines from the European Society of Cardiology (ESC) and the European Respiratory Society (ERS) emphasize a "goal-oriented" treatment strategy. This approach dictates that therapeutic decisions should be guided by a multiparametric risk assessment performed at baseline and during every follow-up visit. The goal is to achieve and maintain a "low-risk" status, which corresponds to a predicted one-year mortality of less than five percent. However, the application of these rigorous stratification tools in clinical practice in the Fergana Valley region faces challenges related to diagnostic resource availability and physician adherence.

At Andijan State Medical Institute, we aimed to validate the utility of systematic risk stratification in our local PAH cohort. Furthermore, we sought to explore the pathophysiological underpinnings of high-risk status. Emerging evidence suggests that the progression of PAH is driven not only by hemodynamic factors but also by systemic metabolic and neurohumoral dysregulation. Therefore, understanding the correlation between clinical risk strata and biological markers is essential for optimizing care. This article presents an analysis of the importance of

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determining risk stratification in PAH patients, focusing on its ability to predict clinical deterioration and guide therapeutic interventions.

## METHODS

Study Design and Participants This prospective observational study was conducted at the Department of Faculty Therapy of Andijan State Medical Institute from January 2024 to January 2025. The study enrolled 54 patients diagnosed with Group 1 Pulmonary Arterial Hypertension (including idiopathic, heritable, and connective tissue disease-associated forms). Inclusion criteria were: mean Pulmonary Arterial Pressure (mPAP) >20 mmHg, Pulmonary Vascular Resistance (PVR) >2 Wood units, and Pulmonary Artery Wedge Pressure (PAWP) ≤15 mmHg assessed by right heart catheterization. Patients with severe comorbidities affecting prognosis independent of PAH were excluded.

Risk Stratification Protocol Patients underwent comprehensive assessment at baseline and at 6 months. We utilized the simplified three-strata risk assessment model proposed by the ESC/ERS guidelines. The parameters included:

- Clinical Signs of Right Heart Failure: Assessment of edema and ascites.
- Symptom Progression: Rate of deterioration.
- WHO Functional Class (WHO-FC): I-IV grading.
- Exercise Capacity: 6-Minute Walk Distance (6MWD).
- Biomarkers: N-terminal pro-brain natriuretic peptide (NT-proBNP).
- Echocardiography: Right atrial area and pericardial effusion presence.

Patients were categorized as Low Risk (green), Intermediate Risk (yellow), or High Risk (red) based on the number of criteria met.

Metabolic Assessment To provide a deeper pathogenetic context, we integrated metabolic monitoring into the risk assessment. Drawing from the work of Tashtemirova [8], who highlighted the state of functional activity of the sympathetic-adrenal system in metabolic syndromes, we assessed markers of sympathetic tone (heart rate variability). Additionally, following the methodology of Juraboyev and Tashtemirova [9], we evaluated lipid peroxidation processes, hypothesizing that oxidative stress correlates with RV dysfunction in PAH. Diagnostic criteria were rigorously reviewed to ensure accurate phenotyping, as recommended by Tashtemirova [10] for complex cardiac syndromes.

Statistical Analysis Data were analyzed using SPSS 26.0. Survival analysis and event-free survival (time to clinical worsening) were calculated using Kaplan-Meier curves. Differences between risk groups were assessed using the Log-rank test.

## RESULTS

Baseline Risk Profile The study population consisted of 54 patients with a mean age of 48.5 ± 12.3 years, predominantly female (65 percent). At baseline, the risk distribution was as follows: 15 percent were Low Risk, 55 percent were Intermediate Risk, and 30 percent were High Risk. This indicates that the majority of patients present at a stage where disease progression is active but potentially reversible with aggressive therapy.

Clinical Outcomes by Risk Strata The prognostic power of the stratification was evident at the 6-month follow-up. Patients who remained in or improved to the Low-Risk category had zero hospitalizations for heart failure and reported significant improvements in quality of life. In contrast, the High-Risk group experienced a 45 percent rate of clinical worsening, defined as the need for hospitalization, escalation to parenteral therapy, or death. The Intermediate-Risk group

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showed a divergent course; those who did not improve despite oral therapy trended towards the high-risk phenotype over time.

Correlation with Metabolic Markers The study revealed a significant association between risk status and metabolic markers. High-Risk patients exhibited significantly elevated levels of malondialdehyde (MDA), a marker of lipid peroxidation, compared to Low-Risk patients. This aligns with the findings of Juraboyev and Tashtemirova [9], suggesting that oxidative stress is a molecular driver of vascular remodeling and RV failure in high-risk states. Furthermore, markers of sympathetic overactivity were most pronounced in the High-Risk and Intermediate-Risk groups, supporting the concept described by Tashtemirova [8] regarding the deleterious role of the sympathoadrenal system in cardiovascular pathology. The persistent sympathetic drive likely contributes to pulmonary vasoconstriction and arrhythmias in these vulnerable patients.

Therapeutic Implications Patients in the Intermediate and High-Risk groups required treatment escalation. The study showed that transitioning patients from monotherapy to initial or sequential double combination therapy (Endothelin Receptor Antagonist + PDE5 Inhibitor) significantly improved risk scores. However, a subset of patients remained in the intermediate-risk stratum ("grey zone"), representing a therapeutic challenge that may require metabolic modulation in addition to vasodilators.

## DISCUSSION

The findings from Andijan State Medical Institute reinforce the absolute necessity of systematic risk stratification in PAH management. The "traffic light" approach (Green/Yellow/Red) provides a clear roadmap for clinicians.

The Danger of the Intermediate State Our data highlights that the "Intermediate Risk" category is not a stable state but a transitional phase often leading to deterioration. The high prevalence of metabolic derangements in this group suggests that subclinical RV strain is ongoing. As emphasized by Tashtemirova [10], diagnostic criteria must be applied attentively; simply having stable symptoms (WHO-FC II-III) should not be interpreted as treatment success if biomarkers (NT-proBNP) or exercise capacity (6MWD) remain suboptimal.

Metabolic Targets The correlation between risk strata and oxidative stress markers opens new avenues for adjunctive therapy. Standard PAH drugs target vasodilation, but they do not directly address the metabolic crisis of the right ventricle. The work of Juraboyev [9] on lipid peroxidation suggests that antioxidant strategies or metabolic modulators (like trimetazidine) might benefit high-risk PAH patients by preserving RV function. Similarly, addressing the sympathetic hyperactivity noted in Tashtemirova's research [8] through beta-blockade (carefully titrated) or renal denervation could be future research directions for refractory PAH.

Local Implementation Implementing this stratification allows for the rational allocation of resources. High-risk patients can be prioritized for expensive parenteral therapies or referral for transplant assessment, while low-risk patients can be managed with oral combinations and less frequent monitoring.

## CONCLUSION

The clinical study conducted at the Department of Faculty Therapy of Andijan State Medical Institute leads to the following conclusions regarding the management of Pulmonary Arterial Hypertension:

Prognostic Validity: Multiparametric risk stratification is a highly reliable predictor of survival and hospitalization-free survival in the local PAH population. Achieving a Low-Risk status is the only acceptable therapeutic goal.

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Metabolic Link: High-risk status is intrinsically linked to systemic metabolic dysregulation, characterized by intense lipid peroxidation and sympathetic overactivity, which likely fuels disease progression.

Treatment Strategy: Regular risk assessment must drive therapeutic inertia; patients in the intermediate or high-risk strata require immediate escalation of therapy rather than maintenance of the status quo.

Therefore, we recommend the mandatory integration of the ESC/ERS risk stratification table into the electronic or paper medical records of all PAH patients in specialized centers to ensure evidence-based, goal-oriented care.

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