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Original Article

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Prevalence and Predictors of Mortality in ICU Patients with Pulmonary Hypertension and Right Ventricular Failure: A Retrospective Cross-Sectional Study

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Abstract

Background: Right Ventricular Failure (RVF) represents a severe complication of Pulmonary Hypertension (PH) with substantial mortality, particularly in Intensive Care Unit (ICU) settings. This study aimed to determine the prevalence of echocardiographically assessed RVF and identify mortality predictors in ICU-admitted PH patients.

Methods: This retrospective cross-sectional study included 62 adult PH patients admitted to Rasoul Akram Hospital, Tehran, Iran, between March 2023 and March 2024. RV function was assessed using echocardiographic parameters, including Right Atrial Pressure (RAP), Right Ventricular Fractional Area Change (RVFAC), Tricuspid Annular Plane Systolic Excursion (TAPSE), and Right Ventricular Myocardial Performance Index (RVMPI). Clinical, laboratory, and outcome data were analyzed using SPSS version 26. Cox regression was performed to identify mortality predictors. Data on clinical demographics, laboratory findings (creatinine, sodium, hemoglobin, albumin, potassium), comorbidities, and outcomes were evaluated using SPSS v26. Mortality predictors were identified through Cox regression analysis.

Results: All patients (100%) demonstrated echocardiographic evidence of RV dysfunction. In-hospital mortality was 41.9% (26 patients). ICU stays were significantly longer among non-survivors than survivors (26.88 *vs*. 11.97 days; p=0.001). Mean RAP, RVFAC, and TAPSE were 8.71±4.7 *mmHg*, 31.5±7.5%, and 15.9±3.9 *mm*, respectively. Independent mortality predictors included older age (HR=1.03; p=0.002), hyponatremia (HR=2.89; p<0.001), elevated creatinine (HR=1.25; p=0.001), RAP >8 *mmHg* (HR=1.78; p=0.003), ICU stay >20 days (HR=3.14; p<0.001), and chronic kidney disease (HR=2.10; p=0.002).

Conclusion: RV dysfunction was prevalent in all ICU-admitted PH patients, with an in-hospital mortality rate of 41.9%. Older age, hyponatremia, renal dysfunction, elevated RAP, and prolonged ICU stay were associated with increased mortality. Early recognition and management of these factors may improve outcomes.

Keywords: Echocardiography, Intensive care units, Pulmonary hypertension, Risk factors, Right ventricular failure

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Introduction

Pulmonary hypertension refers to an abnormal increase in pressure within the pulmonary arteries. Historically, the diagnosis was based on a resting mean Pulmonary Artery Pressure (mPAP) of 25 *mmHg* or higher, as outlined in earlier guidelines. This threshold served as the primary reference for diagnosing the condition for many years. However, following updates from the Sixth World Symposium on Pulmonary Hypertension in 2022, the definition has been revised (1). The new diagnostic cutoff for mPAP is now set at levels above 20 *mmHg*. This change is based on research indicating that even slight elevations in PAP can be associated with clinical complications. To diagnose Pulmonary Arterial Hypertension (PAH), additional criteria must also be considered. Pulmonary Capillary Wedge Pressure (PCWP) should be 15 *mmHg* or lower to exclude issues stemming from left heart disorders. Furthermore, Pulmonary Vascular Resistance (PVR) must exceed 2 *Wood* units, which signifies narrowing or blockage within the pulmonary vessels. In cases where mPAP ranges between 21 and 24 *mmHg*, the patient may be categorized as Borderline Pulmonary Hypertension (Borderline PH), warranting closer monitoring and follow-up care. Early detection and effective treatment are vital to improving patients' quality of life and mitigating complications related to this condition (2). Pulmonary hypertension remains a significant health concern worldwide, affecting people across all age groups, with an especially pronounced impact on the growing population of elderly individuals. It demonstrates higher prevalence in countries with older populations, exerting substantial pressure on healthcare systems. Current statistics estimate that approximately 1% of the global population is affected by pulmonary hypertension, with this figure increasing to nearly 10% among those aged 65 and older (2,3).

Despite variations in the underlying causes and treatment approaches for different forms of pulmonary hypertension, this condition holds significant clinical importance across all cases. It commonly manifests through symptoms such as shortness of breath, chronic fatigue, and a reduced ability to carry out everyday activities. Furthermore, it almost invariably presents an elevated risk of mortality, particularly if timely and appropriate diagnosis or treatment is not achieved. With the increasing elderly population in many countries, pulmonary hypertension has emerged as a growing challenge for healthcare systems. This highlights the critical need for public awareness, early diagnosis, and unhindered access to effective treatments (4).

Right Ventricular Failure (RVF) stands out as a key prognostic factor in patients with pulmonary hypertension, accounting for over 70% of disease-related deaths. Hemodynamically, this condition is characterized by a reduction in cardiac index (below 2.5 liters per minute per square meter-$L/min/m^2$) and elevated Right Atrial Pressure (RAP exceeding 8 *mmHg*). However, the absence of a standardized global definition has complicated the assessment of this dysfunction in clinical studies and trials. The pathophysiology of RVF primarily stems from a sudden increase in afterload due to PVR and impaired synchronization between the Right Ventricle and the Pulmonary Artery (RV-PA uncoupling). This disruption can be quantified through a reduced ratio of maximal pressure-volume change during systole (Ees/Ea) (5,6).

PH is a major reason for Intensive Care Unit (ICU) admissions, presenting significant challenges for physicians. Although medical care has advanced, the prevalence and effects of RVF in these patients are still not fully understood. The combination of PH and RVF creates complex diagnostic and treatment hurdles, often linked to high mortality rates. Comorbidities and common hemodynamic instability further reduce survival chances, especially in patients with poor prognosis (7,8).

This study aimed to evaluate the prevalence of RVF, specifically utilizing echocardiography, in ICU patients experiencing elevated pulmonary pressure levels. By addressing this critical issue, the research seeks to enhance our understanding of the cardiovascular complications linked to PH within intensive care environments, ultimately aiding in improved patient outcomes and the development of more effective management strategies.

Materials and Methods

This retrospective cross-sectional study took place in the ICU of Rasoul Akram Hospital in Tehran, Iran, spanning March 2023 to March 2024. This

retrospective cross-sectional study consecutively enrolled adult patients (age ≥18 years) admitted to the ICU with a proven diagnosis of PH according to accepted clinical and radiological criteria. Patients would only be considered if a full echocardiogram had been done within the first 24 *hrs* of ICU admission. In order to obtain a uniform population group in this retrospective analysis that could reduce any variables that could act as confounders, those patients who had one of the following characteristics were excluded: severe left ventricular systolic dysfunction (ejection fraction <40%); uncorrected congenital heart disease; severe non-cardiac conditions that are deemed to be in the terminal phase, such as metastatic cancer; incomplete medical history/critical data missing. RVF was evaluated within 24 *hr* of ICU admission using echocardiographic measurements, which included RAP, Right Ventricular Fractional Area Change (RVFAC), Right Ventricular Systolic Pressure (RVSP), Tricuspid Annular Plane Systolic Excursion (TAPSE), and the Right Ventricular Myocardial Performance Index (RVMPI).

Data on demographics, laboratory parameters (creatinine, sodium, hemoglobin, albumin, potassium), and clinical outcomes such as mortality and ICU length of stay were collected from medical records. Statistical analyses were conducted using SPSS version 26, applying Student'T tests, ANOVA, and chi-square tests for group comparisons. Additionally, Cox regression modeling was used to identify predictors of mortality, with a significance threshold set at $p<0.05$. Ethical approval for the study was granted by Iran University of Medical Sciences (IR.IUMS.FMD.REC.1403.006).

Results

The study analyzed a comprehensive dataset of patients, presenting a mean age of 72.29±13.99 years with an age range spanning from 23 to 92 years. This cohort included a majority of females, accounting for 58.1% (n=36), while males represented 41.9% (n=26). Demographic and socioeconomic details revealed that most participants had limited educational backgrounds, with 90.3% not exceeding a high school diploma level. Additionally, income levels predominantly fell within the low-to-moderate range, reported by 83.9% of the participants (Table 1).

Table 1. Demographic and socioeconomic characteristics

Variable	Category	n (%)
Sex	Female	36(58.1%)
	Male	26(41.9%)
Education	Primary school	26(41.9%)
	High school diploma	18(29.0%)
	No formal education	12(19.4%)
	University degree	6(9.7%)
Occupation	Homemaker	27(43.5%)
	Unemployed	23(37.1%)
	Self-employed	12(19.4%)
Income level	Low	17(27.4%)
	Moderate	35(56.5%)
	Good	7(11.3%)
	Very good	3(4.8%)

Regarding comorbidities, hypertension was observed as the most common condition, affecting 43.5% of the cohort, while diabetes mellitus showed nearly similar prevalence at 41.9%. In contrast, rarer conditions such as scleroderma and endocarditis were documented in only 3.2% and 1.6% of individuals, respectively (Table 2). In particular, this study population did not include subjects with PH secondary to Congenital Heart Disease (CHD-PH). Unfortunately, due to the retrospective nature of the present study based on ICU admission records, reliable data regarding the exact date of initial PHTN diagnosis or the duration of symptoms prior to admission was not consistently available for the entire cohort. Therefore, this specific parameter could not be included in our analysis.

Echocardiographic evaluations uniformly confirmed the presence of RVF among all patients. Laboratory assessments yielded key findings, including an elevated serum creatinine level (2.14±1.95 *mg/dL*) alongside hyponatremia (mean sodium concentration of 136.76±7.55 *mmol/L*), with Chronic Kidney Disease (CKD) detected in 27.4% of cases (Table 3). Echocardiographic studies further highlighted severe PH, as evidenced by elevated RVSP (RVSP: 45.35± 10.64 *mmHg*). Indicators of impaired right ventricular function were noted, such as reduced TAPSE (TAPSE: 15.86±3.89 *mm*; with half of the samples

Table 2. Comorbidities

Condition	n (%)
Hypertension (HTN)	27(43.5%)
Diabetes Mellitus (DM)	26(41.9%)
Chronic Kidney Disease (CKD)	17(27.4%)
Ischemic Heart Disease (IHD)	15(24.2%)
Chronic Obstructive Pulmonary Disease (COPD)	11(17.7%)
Congestive Heart Failure (CHF)	8(12.9%)

Table 3. Laboratory parameters

Parameter	Mean±SD	Range
Creatinine	2.14±1.95 *mg/dL*	0.6-10.6 *mg/dL*
Sodium	136.76±7.55 *mmol/L*	115-162 *mmol/L*
Hemoglobin	10.72±2.71 *g/dL*	5.117.2 *g/dL*

below the critical threshold of 17 *mm*) and increased RAP (RAP: 8.71±4.70 *mmHg*) (Table 4).

Hospitalization outcomes showed a mortality rate of 41.9% (n=26), with non-survivors experiencing significantly prolonged ICU stays compared to survivors (26.88±16.82 days *vs*. 11.97±6.47 days; p=0.001). As per the pre-defined exclusion criteria, none of the patients with PH linked to congenital heart diseases were included in the final analysis. Moreover, as a result of the retrospective nature of this study, data on the exact duration of PH prior to ICU admission was not possible to obtain. Moreover, as this particular study revealed the predictors of mortality, the final cause of the deaths could not be formally adjudicated in this particular analysis.

While no significant differences were detected between survivors and non-survivors concerning laboratory or echocardiographic parameters (p>0.05 in all cases) (Tables 5 and 6). Data on demographics, laboratory values (creatinine, sodium, hemoglobin, albumin, potassium), and clinical outcomes including in-hospital mortality and ICU length of stay was obtained. Data on the exact duration of pulmonary hypertension prior to ICU admission wasn't available in a systematic way, hence wasn't collected either

Table 4. Echocardiographic parameters

Parameter	Mean±SD	Abnormal threshold
RSVP	45.35±10.64 *mmHg*	>35 *mmHg*
TAPSE	15.86±3.89 *mm*	<17 *mm*
RAP	8.71±4.70 *mmHg*	>8 *mmHg*

Right Ventricular Systolic Pressure (RVSP), Tricuspid Annular Plane Systolic Excursion (TAPSE), Right Atrial Pressure (RAP).

Table 5. ICU stay duration by outcome

Group	No.	ICU stay (days)	p-value
Non-survivors	26	26.88±16.82	0.001
Survivors	36	11.97±6.47	-

Table 6. Echocardiographic comparison by outcome

Parameter	Non-survivors	Survivors	p-value
RAP (*mmHg*)	7.88±4.51	9.31±4.80	0.239
TAPSE (*mm*)	16.58±2.96	15.33±4.41	0.189

Cox regression analysis identified six independent mortality predictors in this patient population. These predictors were as follows: advancing age [Hazard Ratio (HR): 1.03 per year; confidence interval [CI]: 1.01-1.05; p=0.002], presence of hyponatremia defined as serum sodium ≤136 *mmol/L* (HR: 2.89; CI: 1.56-5.35; p<0.001), elevated serum creatinine levels (HR: 1.25 per *mg/dL*; CI: 1.10-1.42; p=0.001), RAP exceeding 8 *mmHg* (HR: 1.78; CI: 1.22-2.60; p=0.003), ICU stays longer than 20 days (HR: 3.14; CI: 1.92-5.14; p<0.001), and the presence of CKD (HR: 2.10; CI: 1.30-3.40; p=0.002) (Table 7).

These findings underline critical clinical factors influencing patient outcomes, providing valuable insights into risk stratification and management strategies in individuals with severe right heart dysfunction complicated by PH and associated comorbidities.

Table 7. Mortality predictors (cox regression)

Predictor	HR (95%CI)	p-value
Age (per year)	1.03(1.01-1.05)	0.002
Hyponatremia (Na ≤136 *mmol/L*)	2.89(1.56-5.35)	<0.001
Creatinine (per *mg/dL*)	1.25(1.10–1.42)	0.001
RAP >8 *mmHg*	1.78(1.22–2.60)	0.003
ICU stay >20 days	3.14(1.92–5.14)	<0.001
Chronic kidney disease	2.10(1.30–3.40)	0.002

Discussion

This study aimed to identify predictors of mortality in patients with RVF caused by PH. The findings revealed that factors such as advanced age, hyponatremia, elevated serum creatinine levels, high RAP, prolonged hospital stays, and CKD are independent risk factors for mortality. These outcomes were analyzed within the context of previous studies and associated pathophysiological mechanisms. Age was found to correlate with a 3% higher mortality risk per additional year (HR=1.03). This result reflects reduced physiological reserves, increased comorbidities such as diabetes, and weakened immune function in elderly patients. The finding aligns with prior research, including a study by Campo *et al* (9) which reported higher mortality rates among older patients with PH caused by Connective Tissue Disease (CTD). This underscores the importance of thorough screening and more aggressive management strategies for the elderly population.

Hyponatremia emerged as one of the strongest risk factors (HR=2.89). Other studies have similarly linked hyponatremia with increased mortality risk. This condition may mirror the activation of the Renin-Angiotensin-Aldosterone System (RAAS), leading to fluid retention, exacerbation of RVF, and reduced renal blood flow. The result parallels findings by Haddad *et al* (10) who reported a 3.6-fold increased risk of 90-day mortality linked to hyponatremia. Excessive RAAS activity and elevated vasopressin levels could contribute to fluid retention, worsening RV dysfunction, and diminished kidney perfusion. These mechanisms suggest that correcting hyponatremia could help improve hemodynamics. Elevated serum creatinine levels (HR=1.25) and CKD (HR=2.10) were also identified as significant predictors (11).

Research by Aronson *et al* (12) has shown that renal dysfunction is associated with increased production of inflammatory cytokines (*e.g.*, IL-6, TNF-α) and the accumulation of uremic toxins, both of which contribute to myocardial damage and RV failure. Additionally, CKD may reduce patients' responsiveness to standard PH treatments, such as PDE-5 inhibitors. High RAP (HR=1.78) indicates impaired RV function and elevated volume load. This finding agrees with previous studies, such as Cassady *et al* (13) which linked elevated RAP to myocardial ischemia and apoptotic pathway activation. Increased RAP can exacerbate blood pooling in venous compartments and impair the function of various organs.

Prolonged hospital stays (HR=3.14) were identified as an independent risk factor for mortality. Extended hospitalization might result from hospital-acquired infections like ventilator-associated pneumonia, deep vein thromboses, or muscle weakness due to immobility. Prolonged stays could also indicate resistance to treatment in some patients.

The outcomes of this study overlap significantly with earlier research in several areas. First, the importance of hyponatremia and renal dysfunction, as confirmed by findings from Campo *et al* and Haddad *et al* (10,14) underscores their critical predictive role. Second, RAP's significance, previously highlighted by Aronson *et al* (12) continues to emphasize its value in assessing RV function. However, this study places unique emphasis on prolonged hospital stays as a strong independent risk factor—an area warranting further exploration.

Given these results, frequent monitoring of electrolytes (especially sodium), the utilization of kidney biomarkers for early diagnosis, preventive strategies to reduce hospital stays, and continuous evaluation of hemodynamics appear crucial in improving outcomes for these patients.

Several limitations should be acknowledged. The relatively small sample size (62 patients) may have hampered the identification of risk factors with smaller effects. In addition, the study did not

assess the influence of specific PH treatments, such as prostacyclin analogs, on clinical outcomes. Furthermore, detailed information regarding underlying causes of PH—such as connective tissue disorders or congenital defects—was lacking.

Conflict of Interest

Authors declare no conflict of interest.

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