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Research

The Prognostic Impact of Acute Kidney Injury in Patients with Moderate and Low-Risk Pulmonary Embolism

Orta ve Düşük Riskli Pulmoner Emboli Hastalarında Akut Böbrek Hasarının Prognostik Etkisi

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ABSTRACT

Objective: This study aimed to evaluate the incidence of acute kidney injury (AKI) and its impact on prognosis in patients diagnosed with acute pulmonary embolism (PE).

Methods: Patients hospitalized with a diagnosis of acute PE between January 2018 and March 2023 were retrospectively reviewed. Demographic data; comorbidities; risk factors such as atrial fibrillation, malignancy, immobilization, history of surgery, fracture, and deep vein thrombosis (DVT); biochemical parameters; and 30-day mortality were recorded. AKI was diagnosed using the kidney disease: improving global outcomes criteria.

Results: AKI was identified in 11.8% of the 186 patients. Compared with those without AKI, patients with AKI were older (p=0.024) and had a higher prevalence of diabetes, chronic kidney disease, atrial fibrillation, and immobilization (p=0.035, 0.001, 0.027, and <0.001, respectively). In the AKI group, serum creatinine and troponin levels were higher, while estimated glomerular filtration rate and serum albumin levels were lower. In the mortality group, comorbidities such as diabetes mellitus, malignancy, immobilization, concomitant DVT, and a simplified pulmonary embolism severity index score ≥1 were observed more frequently. However, there was no significant difference in mortality between patients with and without AKI at admission or during hospitalization (p=0.079).

Conclusion: Among patients with acute PE, AKI present at admission does not independently affect 30-day mortality. However, the occurrence of AKI at admission or during hospitalization was associated with a non-significant trend toward increased mortality (p=0.079).

Keywords: Acute kidney injury, pulmonary embolism, mortality

ÖZ

Amaç: Bu çalışmanın amacı akut pulmoner emboli (PE) tanısı almış hastalarda akut böbrek hasarı (ABH) insidansını ve prognoz üzerindeki etkisini değerlendirmektir.

Gereç ve Yöntem: Ocak 2018 ile Mart 2023 arasında akut PE tanısıyla hastaneye yatırılan hastalar retrospektif olarak incelendi. Demografik veriler, eşlik eden hastalıklar, atriyal fibrilasyon, malignite, immobilizasyon, cerrahi öyküsü, kırık ve derin ven trombozu (DVT) gibi risk faktörleri, biyokimyasal parametreler ve 30 günlük mortalite durumları kaydedildi. ABH, böbrek hastalığı: küresel sonuçları iyileştirme kriterleri kullanılarak teşhis edildi.

Bulgular: Yüz seksen altı hastanın %11,8'inde ABH tespit edildi. ABH olmayan hastalarla karşılaştırıldığında, ABH olan hastalar daha yaşlıydı (p=0,024) ve diyabet, kronik böbrek hastalığı, atriyal fibrilasyon ve immobilizasyon prevalansı daha yüksekti (sırasıyla p=0,035, 0,001, 0,027 ve <0,001). ABH grubunda, serum kreatinin ve troponin seviyeleri daha yüksekken, tahmini glomerüler filtrasyon hızı ve serum albümin seviyeleri daha düşüktü. Mortalite görülen grupta diyabet, malignite, immobilizasyon, eş zamanlı DVT ve basitleştirilmiş pulmoner emboli şiddet indeksi ≥1 daha fazla görüldü. Ancak, ABH olan ve olmayan hastalar arasında hastaneye yatışta ve/veya yatış sırasında mortalite açısından anlamlı bir fark yoktu (p=0,079).

Sonuç: Akut PE hastalarında başvuru anında ABH'nin 30 günlük mortalite üzerine doğrudan bir etkisi görülmemiştir. Ancak başvuru anında ve/veya hastanede yatış sırasında ABH gelişimi, mortaliteyi artırma eğiliminde olmasına rağmen bu artış istatistiksel olarak anlamlı değildir (p=0,079).

Anahtar Kelimeler: Akut böbrek hasarı, pulmoner emboli, mortalite

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INTRODUCTION

Acute kidney injury (AKI), defined as a rapid and often reversible decline in kidney function, is characterized by decreased urine output or elevated serum creatinine (SCr) levels. It is a prevalent condition, particularly among hospitalized patients (1). The incidence of AKI in hospitalized patients is approximately 10-15%, increasing to as high as 50% in those admitted to intensive care units (2).

Pulmonary embolism (PE), a clinical condition caused by partial or complete obstruction of the pulmonary artery or its branches by a thrombus, is the third most common cardiovascular cause of death worldwide (3). The clinical spectrum of PE ranges from asymptomatic cases to fatal outcomes due to hemodynamic instability. In acute PE cases, risk assessment is the most crucial step for appropriate treatment planning, where "risk" refers to mortality. Stratifying patients diagnosed with acute PE into high, intermediate-, or low-risk categories for early mortality directly influences treatment options (anticoagulation or reperfusion) and prognosis (4). The main clinical manifestation of cardiovascular collapse due to massive PE and acute right ventricular failure is hypotension. Patients presenting with persistent hypotension and cardiogenic shock are considered high-risk because these conditions are directly associated with early mortality (5). In patients without detected hypotension or shock, risk assessment using the simplified pulmonary embolism severity index (sPESI) after diagnosis helps identify low- and intermediate-risk patients. Patients with PESI class I-II or sPESI <1 are deemed low-risk, while those with PESI class III-IV or sPESI ≥1 are considered medium risk (6).

AKI can develop in patients with acute PE due to renal congestion, hemodynamic instability, or both. A study by Murgier et al. (7) has shown that the presence of AKI in PE patients is associated with increased mortality across all risk groups (high, medium, and low). Additionally, when AKI status is added to the sPESI score, it enhances mortality prediction and can be useful in deciding whether low-risk patients can be treated at home (7).

In our study, we aimed to determine the frequency of AKI at admission and during hospitalization among medium- and low-risk patients with acute PE, and to investigate the impact of AKI on their prognosis.

METHODS

Patients admitted to the pulmonology department with a diagnosis of hemodynamically stable acute PE between January 2018 and March 2023 were retrospectively reviewed. Patients aged 18 years or older with a confirmed diagnosis of PE by computed tomography pulmonary angiography or ventilation/perfusion scintigraphy were included in the study. Patients with PE who were hemodynamically unstable were excluded from the study because they required monitoring in the intensive care unit. Additionally, patients with missing data, patients with an uncertain diagnosis of embolism, patients with duplicate records, and patients undergoing hemodialysis were excluded from the study (Table 1). Patients' demographic characteristics, comorbidities, risk factors, presence of deep vein thrombosis (DVT), sPESI scores, vital signs, creatinine, estimated glomerular filtration rate (eGFR), albumin, D-dimer, troponin values, and 30-day mortality status were recorded. The eGFR was calculated using the formula provided by the Chronic Kidney Disease Epidemiology Collaboration (8). The diagnosis of AKI was established according to the kidney disease: improving global outcomes (KDIGO) guidelines (9). The presence of AKI at hospital admission and its development during hospitalization were documented.

The sPESI is calculated based on six clinical parameters: age >80 years, history of cancer, chronic cardiopulmonary disease, heart rate ≥110 bpm, systolic blood pressure <100 mmHg, and oxygen saturation <90%. Patients with an sPESI score of 0 are considered low risk, whereas those with a score ≥1 are considered high risk.

In accordance with the Turkish Thoracic Society Pulmonary Embolism Consensus Report, patients were further categorized into moderate- and low-risk groups. Specifically, those with a PESI class I-II or sPESI <1 were categorized as low-risk, while patients with a PESI class III-IV or sPESI ≥1 were classified as moderate-risk. It is important to emphasize that these classification systems are exclusively applicable to hemodynamically stable patients (10).

Early-period mortality was defined as death due to any cause occurring within 30 days. Patients were divided into two groups: those with AKI at the time of admission and those without, Additionally, patients were categorized as survivors or non-survivors.

This study was conducted in accordance with the Declaration of Helsinki and was approved by our University of Health

Table 1. Patient selection and exclusion criteria

Patients initially assessed for eligibility	n=343
Patients with missing data excluded)	n=32
Uncertain diagnosis of embolism (excluded)	n=72
Patients with duplicate records (excluded)	n=46
Undergoing hemodialysis (excluded)	n=7
Total number of included patients	n=186

Sciences Türkiye, Kartal Dr. Lütfi Kırdar City Hospital Clinical Research Ethics Committee (approval no: 2022/514/238/20, date: 29.11.2022).

Statistical Analysis

Continuous data are presented as median and interquartile range (IQR). Categorical data are presented as percentages. For multiple-group comparisons of categorical variables, the chi-square test was used. Continuous variables were compared using the Mann-Whitney U test. Multivariate logistic regression analysis was performed to identify risk factors associated with mortality. Variables were selected for regression analysis based on the Mann-Whitney U test ($p<0.1$). All tests were performed using SPSS for Windows, version 17.0 (SPSS Inc., Chicago, IL, USA). P-values of less than 0.05 were considered statistically significant.

RESULTS

The study included 186 patients, of whom 82 (44.1%) were male. The average age of the patients was 63 years, and at the time of admission, 22 patients (11.8%) had AKI. The most common comorbidities were hypertension (44.1%), diabetes (23.1%), and coronary artery disease (16.7%), in that order. Active malignancy was present in 62 patients (33.3%). Atrial fibrillation was detected in 18 (9.7%) patients and DVT in 70 (39.5%) patients at the time of admission (Table 2).

The group with AKI at admission had a significantly higher mean age (p=0.024). Additionally, diabetes, chronic kidney disease, chronic atrial fibrillation, and immobilization were more frequent (p=0.035, p<0.001, p=0.027, p<0.001, respectively). Vital signs indicated that the group with AKI had lower oxygen saturation and pulse rate (p=0.025 and p=0.022, respectively) (Table 2).

In the group with AKI at admission, SCr and troponin levels were significantly higher, and eGFR and serum albumin levels were lower (p<0.000, p=0.002, p<0.000, p=0.003, respectively) (Table 3).

Among patients who died within 30 days, diabetes, active malignancy, immobilization, concurrent DVT, and a sPESI score ≥1 were significantly more common than in the group that did not die (p=0.037, p=0.007, p=0.039, p=0.048, and p=0.005, respectively). Mortality was higher in the group with AKI at admission or during hospitalization, although the difference was not statistically significant (p=0.079). Vital signs indicated that the group who died had a higher pulse

Table 2. Baseline characteristics of pulmonary thromboembolism patients according to AKI presence at admission

	All patients (n=186) median (IQR)	No AKI (n=164) median (IQR)	AKI (n=22) median (IQR)	p-value
Age (years)	63 (50-76)	62 (49-75)	73 (60.5-80.5)	**0.024**
Gender (male), n (%)	82 (44.1)	76 (46.3)	6 (27.3)	0.091
Comorbidities				
Hypertension, n (%)	82 (44.1)	70 (42.7)	12 (54.5)	0.293
Diabetes mellitus, n (%)	43 (23.1)	34 (20.7)	9 (40.9)	**0.035**
Coronary artery disease, n (%)	31 (16.7)	28 (17.1)	3 (13.6)	1.000
Chronic kidney disease, n (%)	21 (11.3)	14 (8.5)	7 (31.8)	**0.001**
Previous stroke, n (%)	15 (8.1)	12 (7.3)	3 (13.6)	0.271
Atrial fibrillation, n (%)	18 (9.7)	13 (7.9)	5 (22.7)	**0.027**
Malignancy, n (%)	62 (33.3)	51 (31.1)	11 (50)	0.077
Immobilization, n (%)	72 (38.7)	56 (34.1)	16 (72.7)	**0.000**
History of surgery n (%)	24 (12.9)	22 (13.4)	2 (9.1)	0.744
Fracture of lower limb n (%)	11 (5.9)	11 (6.7)	0 (0)	0.367
Coexistence with DVT, n (%)	70[a] (39.5)	61 (38.9)	9 (45)	0.596
Physical examination findings				
sBP, mmHg	115 (100-130)	119 (100-130)[b]	112 (100-122.5)	0.318
dBP, mmHg	70 (60-80)	70 (60-80)	70 (60-70)	0.189
Pulse, /min	85.5 (84-97)	85.5 (77.8-99)	77 (70-87.3)	**0.022**
SpO_2	94 (90-96)	95 (90-96)	90.5 (87.5-95)	**0.025**

Values are expressed as median (IQR), count (percentage).
[a]: Nine values were missing, [b]: Three values were missing, AKI: Acute kidney injury, DVT: Deep venous thrombosis, sBP: Systolic blood pressure, dBP: Diastolic Blood pressure, SpO_2: Pulse oximeter oxygen saturation, IQR: Interquartile range

rate (p=0.004), and biochemical parameters showed lower albumin and higher troponin T levels (p<0.000, p=0.009, respectively) (Table 4).

Logistic regression analysis of variables associated with mortality found that only concurrent malignancy was an independent risk factor [p=0.044; 95% confidence interval (CI), 1.04-25.76] (Table 5).

Table 3. Laboratory values of patients admitted with pulmonary embolism according to AKI presence at admission

	All patients (n=186) median (IQR)	No AKI (n=164) median (IQR)	AKI (n=22) median (IQR)	p-value
Serum creatinine, mg/dL	0.83 (0.66-1.04)	0.78 (0.65-0.97)	1.34 (1.07-1.67)	0.000
eGFR, mL/min/1.73 m^2	90.2 (69.8-105.4)	91.6 (77.6-106.4)	40.9 (32.6-61.1)	0.000
Albumin, g/dL	3.6 (3-4)	3.6 (3.1-4.03)	3.3 (2.8-3.5)	0.003
Troponin T, ng/L	19.5 (8-40)	18 (7-35.5)	40 (17-52)	0.002
D-dimer, µg/L	3875 (2722.5-7652.5)	3640 (2267.5-7487.5)	6295 (3200-13057.5)	0.108

IQR: Interquartile range, AKI: Acute kidney injury, eGFR: Estimated glomerular filtration rate

Table 4. Comparison of the demographic, clinical and laboratory characteristics on admission between patients who survived and who died

Variables	n	Patients who survived median (IQR)	n	Patients who died median (IQR)	p-value
Age (years)	**163**	62 (50-75)	**22**	73 (50.3-79)	0.179
Gender (male)	**163**	69 (42.3)	**22**	13 (59.1)	0.137
Comorbidities					
Hypertension	**163**	72 (44.2)	**22**	9 (40.9)	0.772
Diabetes mellitus	**163**	34 (20.9)	**22**	9 (40.9)	**0.037**
Coronary artery disease	**163**	28 (17.2)	**22**	3 (13.6)	1.000
Chronic kidney disease	**163**	17 (10.4)	**22**	4 (18.2)	0.285
Atrial fibrillation	**163**	15 (9.2)	**22**	3 (13.6)	0.454
Malignancy	**163**	49 (30.1)	**22**	13 (59.1)	**0.007**
Immobilization	**163**	59 (36.2)	**22**	13 (59.1)	**0.039**
Coexistence with DVT	**154**	57 (37.01)	**22**	13 (59.1)	**0.048**
Physical examination findings					
sBP, mmHg	**160**	114.5 (100-130)	**22**	115 (100-140)	0.665
dBP, mmHg	**160**	70 (60-80)	**22**	70 (60-71.3)	0.215
Pulse, min	**157**	82 (72-95)	**22**	94.5 (80-111.8)	**0.004**
SpO_2 <90%	**163**	34 (20.9)	**22**	4 (18.2)	1.000
Laboratory findings					
Serum creatinine, mg/dL	**163**	0.84 (0.68-1.04)	**22**	0.82 (0.63-1.21)	0.973
eGFR, mL/min/1.73 m^2	**163**	90.5 (69.5-105.2)	**22**	85.4 (70.9-108.4)	0.771
Albumin, g/dL	**159**	3.6 (3.2-4)	**20**	2.9 (2.6-3.2)	**0.000**
D-dimer, µg/L	**101**	3770 (2785-7420)	**13**	5680 (2055-12410)	0.533
Troponin T, ng/L	**119**	18 (7-38)	**16**	34 (27-49)	**0.009**
AKI at admission	**163**	19 (11.7)	**22**	3 (13.6)	0.730
AKI (admission and/or during hospitalization)	**137**	21 (15.3)	**19**	6 (31.6)	**0.079**
sPESI ≥1	**162**	87 (53.7)	**21**	18 (85.7)	**0.005**
PAP >25 mmHg	**122**	37 (30.3)	**17**	7 (41.2)	0.368

DVT: Deep venous thrombosis, sBP: Systolic blood pressure, dBP: Diastolic blood pressure, SpO_2: Pulse oximeter oxygen saturation, eGFR: Estimated glomerular filtration rate, AKI: Acute kidney injury, sPESI: Simplified pulmonary embolism severity index score, PAP: Pulmonary artery pressure, IQR: Interquartile range

Table 5. Multivariate logistic regression analyses of risk factors associated with mortality in patients admitted with pulmonary embolism

Variables	Multivariate			
	β	OR	95% CI	p-value
Diabetes mellitus	0.050	1.051	0.269-4.116	0.943
Malignancy	1.645	5.182	1.042-25.759	**0.044**
Immobilization	0.370	1.447	0.337-6.214	0.619
Coexistence with DVT	0.473	1.605	0.423-6.092	0.487
Pulse, min	0.036	1.036	0.994-1.080	0.091
Hypoalbuminemia (alb <3.5 g/dL)	1.863	6.443	0.699-59.403	0.100
Troponin T (ng/L)	-0.002	0.998	0.981-1.016	0.824
AKI (admission or during hospitalization)	1.015	2.761	0.567-13.433	0.208
sPESI ≥1	-0.114	0.892	0.114-6.973	0.914

alb: Albumin, DVT: Deep venous thrombosis, AKI: Acute kidney injury, sPESI: Simplified pulmonary embolism severity ındex, OR: Odds ratio, CI: Confidence interval

DISCUSSION

In our study, AKI present at hospital admission in patients with moderate- and low-risk PE did not affect mortality. The mortality rate was higher in patients who developed AKI at the time of initial admission and/or during hospitalization compared with those without AKI; however, this difference was not statistically significant.

AKI is a significant complication in patients with acute PE and has been associated with adverse clinical outcomes. In our study, AKI was identified in 11.8% of patients. In contrast, Murgier et al. (11) conducted a large-scale study involving 21,131 PE patients and reported that 29.5% developed AKI. Furthermore, their analysis demonstrated that AKI was an independent predictor of 30-day all-cause mortality in PE patients [odds ratio (OR)=1.25, 95% CI: 1.02-1.54] (11). Similarly, a recent meta-analysis by Xing et al. (12) reported that AKI is an independent predictor of poor prognosis in acute PE patients, doubling the overall mortality rate (pooled OR=2.75, 95% CI: 2.45-3.08, p<0.001). However, our study, which included 186 patients with moderate- and low-risk PE, found no significant association between AKI and 30-day mortality (p=0.079). This discrepancy may be attributed to differences in patient populations, PE severity, and sample size between the two studies. While Murgier et al. (11) included high-risk PE patients within a much larger cohort, our study focused solely on hemodynamically stable patients; this difference may explain the lack of statistical significance.

In another recent meta-analysis, Wang et al. (13) reported that renal insufficiency, particularly AKI and severe renal impairment (eGFR <30 mL/min/1.73 m^2), was significantly associated with an increased risk of early mortality in PE patients (pooled OR=2.69, 95% CI: 1.24-5.84, p<0.001). Unlike this meta-analysis, our study, which focused exclusively on AKI as defined by KDIGO criteria, found no significant association between AKI and 30-day mortality (p=0.079). This discrepancy may be attributed to differences in how renal impairment is defined among studies; for example, some studies in the meta-analysis included patients with severe chronic kidney disease (eGFR <30 mL/min/1.73 m^2).

In our study, serum albumin levels were significantly lower in patients with AKI than in those without AKI (p=0.003). Similarly, among patients who died within 30-days, serum albumin levels were significantly lower than in those who survived (p<0.000). Wiedermann et al. (14) published a meta-analysis demonstrating that hypoalbuminemia is an independent risk factor for both the development of AKI (OR=2.34, 95% CI: 1.74-3.14) and AKI-related mortality (OR=2.47, 95% CI: 1.51-4.05).

In the management of acute PE, the most commonly used risk stratification tool to guide treatment decisions and predict short-term mortality is the sPESI. In our study, the 30-day mortality rate among patients with an sPESI score ≥1 was significantly higher than among those with an sPESI score <1 (p=0.005).

The sPESI is a widely used and validated tool for risk stratification in acute PE patients. In our study, patients with an sPESI score ≥1 had significantly higher 30-day mortality than those with an sPESI score of 0 (p=0.005). While our study focused on evaluating the prognostic role of sPESI, a large-scale registry study by Murgier et al. (7), which included 30,532 PE patients from the RIETE database, further investigated the impact of AKI on sPESI-based risk stratification. Their findings demonstrated that AKI significantly increased 30-day mortality in all sPESI-defined risk groups: from 0.46% to 3% in low-risk patients, from 5.4% to 10% in intermediate-risk patients, and from 9.4% to 18% in high-risk patients (7). These results suggest that renal function may play a crucial role in PE prognosis. Although our study did not assess integrating AKI into sPESI scoring, our findings align with existing literature by confirming the prognostic power of sPESI.

Concurrent malignancy in patients hospitalized for acute PE has been associated with a 90% increase in all-cause mortality and a longer hospital stay (15). Malignancy is a well-established risk factor for poor prognosis in patients with PE. In our study, malignancy was identified as the only independent predictor of 30-day mortality in the multivariate logistic regression analysis (OR=5.18, 95% CI: 1.04-25.76, p=0.044). This finding highlights the significant impact of malignancy on mortality risk, even after adjustment for other well-known prognostic factors such as immobilization, DVT, troponin elevation, AKI, and sPESI ≥1; none of these factors were independently associated with mortality in our analysis. Similarly, a large-scale retrospective study by Shalaby et al. (15) found that cancer was associated with a significantly higher in-hospital mortality rate (11.8% vs. 6.6%, OR=1.79, p<0.0001).

Study Limitations

Our study has some limitations. It was a single-center retrospective study with a smaller patient group than reported in the literature. High-risk PE patient groups were not included in our study.

CONCLUSION

Our study demonstrated that in hemodynamically stable patients hospitalized with acute PE, the presence of AKI at admission was not an independent predictor of mortality. Although mortality rates were higher in patients with AKI at admission and/or during hospitalization, this difference did not reach statistical significance Further large-scale prospective studies are needed to better elucidate the prognostic role of AKI in patients with hemodynamically stable PE.

ETHICS

Ethics Committee Approval: This study was conducted in accordance with the Declaration of Helsinki and was approved by our University of Health Sciences Türkiye, Kartal Dr. Lütfi Kırdar City Hospital Clinical Research Ethics Committee (approval no: 2022/514/238/20, date: 29.11.2022).

Informed Consent: Retrospective study.

FOOTNOTES

Authorship Contributions

Surgical and Medical Practices: M.O., S.Ş.C., Concept: B.Z.E., S.Ş.C., Design: B.Z.E., Data Collection or Processing: B.Z.E., S.Ş.C., Analysis or Interpretation: M.O., Literature Search: B.Z.E., M.O., Writing: B.Z.E., M.O.

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