ORIGINAL ARTICLE

MORTALITY PREDICTORS IN ELDERLY INTENSIVE CARE UNIT PATIENTS WITH ACUTE KIDNEY INJURY REQUIRING HEMODIALYSIS

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Abstract

Introduction: The incidence of acute kidney injury is increasing in the elderly. This condition is especially serious during the course of critical illness, and the rate of mortality rises with the condition's increasing severity. We aimed to identify the risk factors for in-hospital, 28-day, and 90-day mortality among elderly patients admitted to the intensive care unit with acute kidney injury requiring dialysis.

Materials and Method: We conducted a retrospective study between January 2011 and December 2019 of patients 65 years of age and older who were hospitalized with acute kidney injury requiring dialysis in the intensive care unit of an internal medicine department.

Results: A total of 144 patients were evaluated, 63 male (43.75%) and 81 female (56.25%). The in-hospital, 28-day, and 90-day mortality rates were 40.9%, 47.2%, and 56.2%, respectively. Sepsis etiology was associated with poor prognosis. In univariate Cox regression analysis, we identified use of inotropes, final C-reactive protein, neutrophil to lymphocyte ratio as mortality predictors at all three time points. Use of inotropes, final C-reactive protein continued to be predictors of mortality in multivariate analysis. Age was not found to be a factor affecting mortality.

Conclusions: Data are limited on the outcomes of elderly patients with acute kidney injury requiring dialysis, but routinely evaluated laboratory parameters in intensive care practice may be predictive of mortality. Our results provide deeper understanding of how these variables interact and contribute to the risk of mortality. Chronological age alone should not be a consideration for hemodialysis.

Keywords: Aged; Critical Care; Hemodialysis; Acute Kidney Injury; Mortality.

INTRODUCTION

Acute kidney injury (AKI) is a serious condition that is observed especially in the course of critical illnesses. A multinational, multicenter prospective study reports septic shock as the condition's most common contributing factor (1). The causes of death in hospitalized patients with AKI have been identified as sepsis, cardiovascular disease (CVD), and malignancy, with pneumonia being reported as the main sequela of sepsis (2). AKI cases requiring hemodialysis are associated with increased mortality and morbidity both in hospital and after discharge (3). In recent years, the incidence of AKI requiring dialysis has increased 10% annually (4). Aging is strongly associated with AKI risk and incidence (4-7), although some contend that the risk of AKI requiring dialysis in the elderly is similar to that of young people. However, the incidence of AKI is increasing faster in young people (8).

Mortality in AKI has been reported at rates ranging from 31%–80%, and the highest mortality has been observed in AKI cases requiring dialysis (9). In the BEST kidney study, advanced age was found to be independently associated with in-hospital mortality in patients with AKI (1), which develops due to the co-occurrence of chronic diseases, structural and functional deterioration of the kidneys, and exposure to nephrotoxic agents (5, 6). The outcomes of patients with AKI requiring dialysis in the elderly population are not entirely clear, and the growing incidence of AKI requiring dialysis in that population makes it critical to identify the risk factors for mortality to support early intervention to improve outcomes. This study aimed to determine the mortality rate and the factors predicting mortality in elderly patients who develop AKI requiring hemodialysis.

MATERIALS AND METHOD

This study was conducted retrospectively on patients followed up from 2011–2019 in the intensive care unit (ICU) of the Department of Internal Medicine of Ege University Faculty of Medicine. The study was approved by Ege University's ethics committee (No. 19-5.2T/69) and adhered to the principles of the Declaration of Helsinki. Elderly patients with AKI requiring dialysis upon admission to ICU or who developed AKI requiring dialysis during hospitalization were included, and all patients or their relatives provided written informed consent. Figure 1

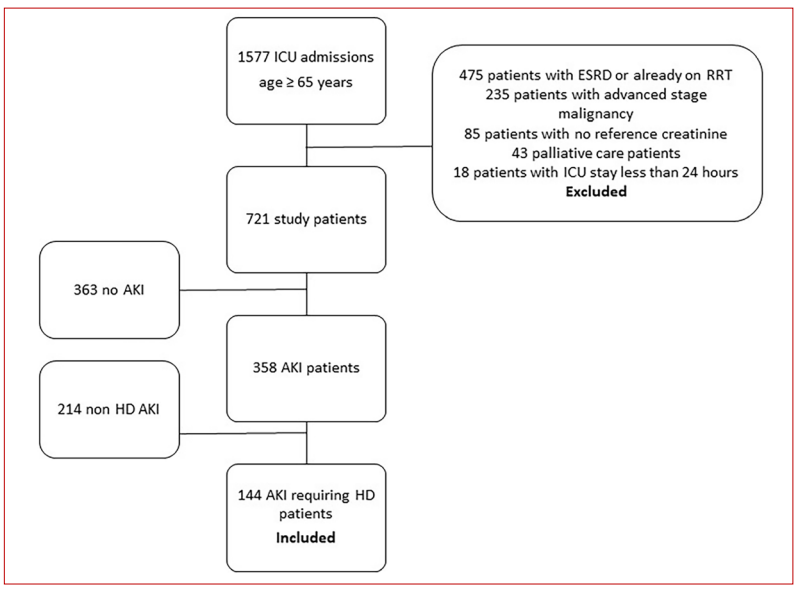

Figure 1. Flow chart of patient inclusion and exclusion

shows a flow chart of patient inclusion and exclusion. *Elderly patients* were defined as those aged 65 years or above (10). Patients were excluded who had a history of end-stage renal disease, were already on renal replacement therapy, were in palliative care, were at an advanced stage of malignancy, died in a period shorter than 24 hours, or had no reference creatinine in the past three months.

Demographic characteristics, comorbidities, AKI etiology, and laboratory data at admission and discharge/death were collected from electronic medical records. The previous diagnosis on clinical records sufficed for the confirmation of comorbidities, including CVD, hypertension (HT), diabetes mellitus (DM), chronic kidney disease (CKD), and heart failure (HF). The Sepsis-3 criterion was used to define sepsis (11), and the Acute Dialysis Quality Initiative consensus report was used to define cardiorenal syndrome (12). We compared survivors and non-survivors to identify the factors associated with mortality. The primary outcome was in-hospital mortality, and the secondary outcomes were mortality at 28 and 90 days after discharge. Deaths were categorized according to the time of occurrence as "in-hospital mortality" if they occurred during intensive care hospitalization, "28-day mortality" if they occurred within the first 28 days after ICU discharge, and "90-day mortality" if they occurred ≥29-90 days after ICU discharge.

Statistical Analysis

The study analyzed various biomarkers, including albumin levels (baseline: 2.76%, follow-up: 5.52%), C-reactive protein levels (baseline and follow-up: 4.83%), neutrophil count (baseline: 0.69%, follow-up: 2.07%), lymphocyte count (baseline: 0.69%, follow-up: 2.07%), urea level (baseline and follow-up: 0.69%), creatinine level (baseline and follow-up: 0.69%), and the neutrophil/lymphocyte ratio (baseline: 0.69%, follow-up: 2.07%). Considering the low variability in these rates (predominantly below 5%) and the likelihood of a near-normal distribution of the data, the mean imputation method was employed for handling missing data. This approach aimed to enhance the credibility of the analytical results by maintaining the integrity of the data set. Mean imputation is particularly beneficial for consistency and validity of analyses when missing data is minimal and under the presumption of negligible inter-variable correlations.

The data presented in Tables 1, 2, and 3 underwent comprehensive analysis, segmented by patient demographic features and clinical conditions. For continuous variables, the analysis employed the mean ± standard deviation for normally distributed data, or the median with minimum and maximum values for non-normally distributed data, contingent upon the data's distribution. Categorical variables were summarized using frequencies and percentages. The normality of numerical variables was ascertained using Shapiro-Wilk, Kolmogorov-Smirnov, and Anderson-Darling tests. The selection of appropriate statistical tests was based on the outcomes of these normality assessments.

For categorical variables, the study utilized Pearson Chi-Square, Fisher's Exact, or Fisher Freeman Halton tests, depending on the number of expected observations, to determine the differences between groups.

In our study, the comparison of numerical variables between two independent groups was conducted using the Independent Samples T-test for variables with normal distribution. Conversely, the Mann-Whitney U test was employed for variables lacking normal distribution.

For the assessment of clinical variables such as NT-proBNP, troponin, mean platelet volume, systolic and diastolic blood pressure, mean arterial pressure, pulse pressure, and heart rate, we utilized the Wilcoxon signed rank test. This approach was specifically chosen for evaluating changes over time in the same patients, comparing measurements at admission (1) and at discharge or death (2). The test's focus was on discerning variations in repeated

measures within individual patients, rather than comparing median values across two independent samples. The application of this test enabled us to statistically analyze the evolution of clinical variables throughout each patient's treatment journey.

In our study, we extensively examined the relationship between mortality rates, including hospital, 28-day, and 90-day mortality, and various clinical variables such as albumin, C-reactive protein (CRP), neutrophils, lymphocytes, urea, creatinine, and the neutrophil/lymphocyte ratio (NLR). This analysis was facilitated by the use of the Nonparametric Analysis of Longitudinal Data in Factorial Experiments (NparLD) package within the R library. The NparLD package is particularly adept at handling non-normally distributed data, which is a characteristic trait of our clinical dataset. This capability is vital for ensuring robust analysis despite the non-normal distribution of our data. Additionally, the package efficiently addresses the complexities associated with longitudinal data, making it an ideal tool for analyzing time-based interactions in our research.

The NparLD package also supports advanced analytical methods, such as F2-LD-F1 and F1-LD-F1 analyses. The F2-LD-F1 analysis is crucial for investigating factorial designs with two factors at two levels, enabling thorough exploration of variable interactions over time. The F1-LD-F1 analysis, on the other hand, is designed for single-factor designs with repeated measures, allowing for detailed assessment of a variable's impact over multiple time points.

Furthermore, we employed key functions of the NparLD package like the Wald-Type Statistic (WTS), ANOVA-Type Statistic (ATS), and Modified ANOVA-Type Statistic in our analysis. These methodologies were instrumental in evaluating the influence of independent variables on the dependent variable, identifying differences between treatment groups, and tracking changes over time. The Modified ANOVA-Type Statistic, in particular, played a critical role in uncovering more complex interactions, with p-values serving as the preferred metric for these outcomes. These capabilities make the NparLD package an invaluable resource for accurately interpreting the intricate relationships among various clinical variables and mortality rates across different time intervals.

In the analysis of the data presented in Tables 5, 6, and 7, it was determined that the Nonparametric Analysis of Longitudinal Data in Factorial Experiments (NparLD) package could not be appropriately applied. The primary limitation stemmed from the extensive amount of missing data within these specific datasets. The NparLD package, while robust in handling complex and non-normally distributed data, requires a relatively complete dataset to effectively analyze longitudinal interactions and factorial designs. Given the significant gaps in the data, particularly in these tables, an alternative approach was deemed more suitable to ensure the accuracy and reliability of our findings. Consequently, we employed other statistical methods that are better equipped to handle such instances of missing data, ensuring that our analysis remained both rigorous and valid despite these data limitations.

In our study, we quantified the temporal impact on mortality using Cox regression analysis. This method involved incorporating variables like etiology, inotrope usage, and biomarkers such as CRP, Mean Platelet Volume (MPV), Creatinine, and Neutrophil counts. These were measured at two key points: baseline (t0) and follow-up (t1). The rationale for selecting these variables was based on theoretical considerations and initial univariate statistical analyses. To bolster the robustness of our model, we evaluated the correlations between these variables at both t0 and t1. This step was crucial to ensure the reliability of our findings and to make the interpretation of each variable's coefficients within the model more clear

and understandable. This approach was carefully chosen to provide a coherent and insightful understanding of how each variable influences mortality over time.

In summary, the NparLD package emerged as a vital tool, meeting the specific demands of our research and yielding results apt for our data structure. The statistical analyses were conducted using Jamovi (version 2.3.28), JASP (version 0.17.3), and R-project (version 4.3.2 for Windows), with a set significance level of 0.05 (p-value) for all statistical tests.

RESULTS

Demographic and Clinical Variable Analysis

In our analysis of demographic and clinical variables, no significant differences were observed between patients who survived hospitalization and those who did not in terms of age, sex, length of hospital stay, rates of discharge on permanent dialysis, and comorbidity rates ($p>0.05$ for each).

Analysis of AKI Etiology and Inotrope Use on Mortality

Regarding the etiologies of Acute Kidney Injury (AKI), sepsis and malignancy-related etiologies were more prevalent in the mortality group, whereas cardiorenal syndrome, exposure to nephrotoxic drugs, and other causes were predominant in the survivors ($p<0.001$). Notably, the use of inotropes was significantly higher in patients who did not survive ($p<0.001$) (referenced in Table 1).

28-Day Mortality Analysis

Focusing on 28-day mortality, our study found no significant variances between the groups in terms of age, sex, hospital stay duration, discharge on permanent dialysis, and comorbidity rates ($p>0.05$ for each). In the comparison of AKI causes, patients who died within 28 days exhibited a higher incidence of sepsis and malignancy-related AKI, while those surviving within this period showed a higher occurrence of cardiorenal syndrome, nephrotoxic drugs, and other causes ($p<0.001$). Again, inotrope usage was significantly more frequent in the mortality group within 28 days ($p<0.001$) (as indicated in Table 2).

90-Day Mortality Analysis

Regarding 90-day mortality, there were no significant differences between the groups concerning age, sex, length of hospital stay, discharge rates with permanent dialysis, and comorbidity rates ($p>0.05$ for each). In contrasting AKI causes, cardiorenal syndrome, sepsis, and malignancy were more frequent in patients who died within 90 days, while nephrotoxic drugs and other causes were more common in the survivors of this period ($p<0.001$). Inotrope use continued to be significantly higher in the mortality group within 90 days ($p<0.001$) (as shown in Table 3).

The Nonparametric Analysis of Longitudinal Data in Factorial Experiments

In terms of hospital mortality, the effects of time interaction with CRP, creatinine, and N/L ratio levels were significant ($p<0.05$ for each), while interactions with albumin, lymphocyte, neutrophil, and urea levels were not significant ($p>0.05$ for each). When analyzing 28-day mortality, we observed no significant time interaction effects with albumin, CRP, and lymphocyte levels ($p>0.05$ for each). However, interactions with neutrophil, urea, creatinine, and N/L levels were significant ($p<0.05$ for each). Similarly, in the 90-day mortality analysis, time interaction effects with albumin, CRP, and lymphocyte levels remained non-significant ($p>0.05$ for each), whereas significant effects were noted with neutrophil, urea, creatinine, and N/L levels ($p<0.05$ for each) (Table 4). (Figure 2, Figure 3 and Figure 4).

Table 1. Hospital Mortality Statistics: Detailed Patient Profile and Clinical Factors

	Hospital Mortality		p
	Alive (n=85)	**Mortality** (n=59)	
Age †	75.3 ± 7.1	74.8 ± 7.3	0.709***
Gender ‡			
Male	35 (41.2)	28 (47.5)	0.564*
Woman	50 (58.8)	31 (52.5)	
Length of Stay §	7.0 [3.0 – 36.0]	8.0 [3.0 – 44.0]	0.747**
Discharge with Permanent Dialysis, yes ‡	14 (16.5)	0 (NaN)	0.999*
Comorbidity ‡			
Diabetes Mellitus, yes	39 (45.9)	24 (40.7)	0.654*
Hypertension, yes	72 (84.7)	44 (74.6)	0.195*
Coronary Artery Disease, yes	34 (40.0)	18 (30.5)	0.322*
Chronic Renal Failure, yes	15 (17.6)	6 (10.2)	0.312*
Chronic Heart Failure, yes	33 (38.8)	25 (42.4)	0.799*
ACI Etiology ‡			
Cardiorenal Syndrome	26 (30.6)	12 (20.3)	**<0.001***
Sepsis	20 (23.5)	31 (52.5)	
Malignancy	11 (12.9)	11 (18.6)	
Nephrotoxic Drugs	15 (17.6)	0 (0.0)	
Other	13 (15.3)	5 (8.5)	
Use of inotropic support, yes ‡	16 (18.8)	38 (64.4)	**<0.001***

Footnote: Table 3 presents data on hospital mortality using various statistical techniques and measurement indicators. The † symbol represents the value as Mean ± Standard Deviation. The ‡ symbol indicates that data are shown in number and percentage format (n (%)). The § symbol signifies that values are presented as median and range [Minimum-Maximum]. The symbols for statistical tests are defined as follows: *. Pearson Chi-Square, Fisher's Exact, or Fisher Freeman Halton test, these tests are used to assess the significance of differences in categorical data across groups. **. Mann-Whitney U test is employed for comparing median values between two independent samples. ***. Independent Samples T-Test is used to compare mean differences between two independent groups. The 'NaN' (Not a Number) value in the table indicates that the data is not available or cannot be calculated.

Table 2. Outcomes: Demographics and Clinical Characteristics

	Overall (n=144)	**28-Day Mortality**		**p**
		Alive (n=76)	**Mortality** (n=68)	
Age †	75.1 ± 7.2	74.8 ± 7.0	75.4 ± 7.4	0.638***
Gender ‡				
Male	63 (43.8)	30 (39.5)	33 (48.5)	0.355*
Woman	81 (56.2)	46 (60.5)	35 (51.5)	
Length of Stay §	7.0 [3.0 – 44.0]	7.0 [3.0 – 44.0]	8.0 [3.0 – 26.0]	0.949**
Discharge with Permanent Dialysis, yes ‡	14 (16.5)	13 (17.6)	1 (9.1)	0.682*
Comorbidity ‡				
Diabetes Mellitus, yes	63 (43.8)	36 (47.4)	27 (39.7)	0.449*
Hypertension, yes	116 (80.6)	64 (84.2)	52 (76.5)	0.337*
Coronary Artery Disease, yes	52 (36.1)	30 (39.5)	22 (32.4)	0.475*
Chronic Renal Failure, yes	21 (14.6)	11 (14.5)	10 (14.7)	0.999*
Chronic Heart Failure, yes	58 (40.3)	28 (36.8)	30 (44.1)	0.472*
ACI Etiology ‡				
Cardiorenal Syndrome	38 (26.4)	22 (28.9)	16 (23.5)	
Sepsis	51 (35.4)	18 (23.7)	33 (48.5)	
Malignancy	22 (15.3)	10 (13.2)	12 (17.6)	**0.001***
Nephrotoxic Drugs	15 (10.4)	14 (18.4)	1 (1.5)	
Other	18 (12.5)	12 (15.8)	6 (8.8)	
Use of inotropic support, yes ‡	54 (37.5)	14 (18.4)	40 (58.8)	**<0.001***

Footnote: In Table 1, various statistical analysis methods and measurement indicators are employed. The † symbol indicates that the provided value represents Mean ± Standard Deviation. The ‡ symbol signifies that the data are presented as number and percentage (n (%)). The § symbol denotes that values are presented as median and range [Minimum-Maximum]. Symbols and their corresponding statistical tests are as follows: *. Pearson Chi-Square, Fisher's Exact, or Fisher Freeman Halton test, these tests are used to determine if there is a significant difference between categorical data across two or more groups. **. Mann-Whitney U test is used to test for differences in median values between two independent samples. ***. Independent Samples T-Test is employed to compare mean differences between two independent groups.

Table 3. 90-Day Mortality Rates: Patient Demographics and Clinical Data Analysis

	90-Day Mortality		p
	Alive (n=63)	**Mortality** (n=81)	
Age †	74.2 ± 6.4	75.8 ± 7.6	0.186***
Gender ‡			
Male	25 (39.7)	38 (46.9)	0.485*
Woman	38 (60.3)	43 (53.1)	
Length of Stay §	7.0 [3.0 – 35.0]	8.0 [3.0 – 44.0]	0.501**
Discharge with Permanent Dialysis, yes ‡	9 (14.3)	5 (22.7)	0.504*
Comorbidity ‡			
Diabetes Mellitus, yes	31 (49.2)	32 (39.5)	0.320*
Hypertension, yes	53 (84.1)	63 (77.8)	0.458*
Coronary Artery Disease, yes	22 (34.9)	30 (37.0)	0.930*
Chronic Renal Failure, yes	6 (9.5)	15 (18.5)	0.201*
Chronic Heart Failure, yes	20 (31.7)	38 (46.9)	0.095*
ACI Etiology ‡			
Cardiorenal Syndrome	14 (22.2)	24 (29.6)	
Sepsis	15 (23.8)	36 (44.4)	
Malignancy	8 (12.7)	14 (17.3)	**<0.001***
Nephrotoxic Drugs	14 (22.2)	1 (1.2)	
Other	12 (19.0)	6 (7.4)	
Use of inotropic support, yes ‡	10 (15.9)	44 (54.3)	**<0.001***

Footnote: Table 2 employs various statistical methods and measurement indicators for analyzing data on 90-day mortality. The † symbol indicates the value is presented as Mean ± Standard Deviation. The ‡ symbol signifies that the data are shown as number and percentage (n (%)). The § symbol denotes values presented as median and range [Minimum-Maximum]. The symbols used for statistical tests and their meanings are: *. Pearson Chi-Square, Fisher's Exact, or Fisher Freeman Halton test, utilized to determine if there is a significant difference in categorical data across different groups. **. Mann-Whitney U test is used for testing differences in median values between two independent samples. ***. Independent Samples T-Test is employed to compare mean differences between two independent groups.

Table 4. Impact of Temporal Changes in Biochemical and Hematological Variables on hospital, 28-Day and 90-Day Mortality

	Hospital Mortality		**Mortality 28**		**Mortality 90**	
	Alive (n=85)	**Mortality** (n=59)	**Alive** (n=76)	**Mortality** (n=68)	**Alive** (n=63)	**Mortality** (n=81)
Albumin 1 §	3.3 [2.0 – 5.2]	3.0 [1.4 – 4.2]	3.3 [1.9 – 5.2]	3.0 [1.4 – 4.2]	3.4 [2.0 – 5.2]	3.0 [1.4 – 4.2]
Albumin 2 §	3.0 [0.3 – 4.5]	2.6 [1.4 – 4.6]	3.1 [0.3 – 4.5]	2.6 [1.4 – 4.6]	3.1 [0.3 – 4.5]	2.6 [1.4 – 4.6]
p (NparLD)**	0.546		0.641		0.549	
C-reactive protein 1 §	7.4 [0.1 – 39.5]	14.1 [1.9 – 39.1]	6.7 [0.1 – 39.5]	13.3 [1.9 – 39.1]	6.7 [0.1 – 37.8]	13.1 [0.3 – 39.5]
C-reactive protein 2 §	4.9 [0.0 – 44.0]	12.4 [0.9 – 69.0]	4.8 [0.0 – 44.0]	12.2 [0.9 – 69.0]	4.7 [0.0 – 44.0]	11.0 [0.9 – 69.0]
p (NparLD)**	**0.040**		0.062		0.089	
Neutrophil 1 §	9990.0 [3.8 – 36050.0]	9620.0 [4.8 – 48290.0]	9695.0 [3.8 – 36050.0]	9690.0 [4.8 – 48290.0]	9330.0 [3.8 – 36050.0]	9880.0 [4.8 – 48290.0]
Neutrophil 2 §	6400.0 [2.1 – 49850.0]	10780.0 [6.2 – 48490.0]	6155.0 [2.1 – 16180.0]	10305.0 [6.2 – 49850.0]	6160.0 [2.1 – 16180.0]	9410.0 [6.2 – 49850.0]
p (NparLD)**	0.035		**0.023**		**0.001**	
Lymphocyte 1 §	980.0 [0.1 – 14100.0]	890.0 [0.3 – 12040.0]	975.0 [0.1 – 14100.0]	945.0 [0.3 – 12040.0]	1170.0 [0.1 – 14100.0]	860.0 [0.3 – 12040.0]
Lymphocyte 2 §	1260.0 [0.3 – 3440.0]	950.0 [0.6 – 3800.0]	1265.0 [0.3 – 3440.0]	960.0 [0.6 – 3800.0]	1300.0 [0.3 – 3440.0]	960.0 [0.6 – 3800.0]
p (NparLD)**	0.432		0.613		0.866	
Urea 1 §	138.0 [17.0 – 429.0]	151.0 [24.0 – 381.0]	128.0 [17.0 – 371.0]	153.0 [24.0 – 429.0]	127.0 [17.0 – 371.0]	153.0 [24.0 – 429.0]
Urea 2 §	99.0 [23.0 – 253.0]	162.0 [46.0 – 436.0]	98.0 [23.0 – 253.0]	149.5 [46.0 – 436.0]	92.0 [23.0 – 253.0]	140.0 [46.0 – 436.0]
p (NparLD)**	0.079		**0.003**		**0.004**	
Creatinine 1 §	4.7 [1.0 – 15.0]	3.7 [0.7 – 10.4]	4.3 [0.7 – 12.3]	4.3 [0.8 – 15.0]	4.7 [1.0 – 12.3]	4.2 [0.7 – 15.0]
Creatinine 2 §	3.1 [0.5 – 9.9]	4.2 [0.6 – 11.9]	2.8 [0.5 – 9.9]	3.8 [0.8 – 11.9]	2.6 [0.5 – 9.9]	3.7 [0.6 – 11.9]
p (NparLD)**	**<0.001**		**0.002**		**<0.001**	
Neutrophil/ Lymphocyte Ratio 1 §	10.1 [0.4 – 97.2]	8.8 [0.1 – 111.3]	9.2 [0.4 – 97.2]	9.6 [0.1 – 111.3]	9.1 [0.4 – 74.8]	10.4 [0.1 – 111.3]
Neutrophil/ Lymphocyte Ratio 2 §	5.9 [0.8 – 28.0]	9.0 [0.5 – 166.8]	5.3 [0.8 – 28.0]	9.3 [0.5 – 166.8]	4.9 [0.8 – 28.0]	8.9 [0.5 – 166.8]
p (NparLD)**	<0.001		<0.001		0.004	

Footnote: In Table 4, the statistical analysis of hospital mortality and mortality at 28 and 90 days is presented. The § symbol indicates that values are represented as median with their respective (§) minimum and maximum range [Min.-Max.]. Data comparisons for albumin, C-reactive protein, neutrophil, lymphocyte, urea, creatinine, and neutrophil/lymphocyte ratio are made between groups 'Alive' and 'Mortality' at different time points (hospital, 28 days, 90 days). The '1' and '2' labels indicate values at admission and at discharge or death, respectively. For statistical comparison, the nonparametric analysis of longitudinal data is conducted using the R software package npaRLD (Nonparametric Analysis of Longitudinal Data in Factorial Experiments). The p** symbol denotes the significance levels determined by the nonparametric longitudinal data analysis (NparLD), providing a robust method for comparing medians across groups and time points.

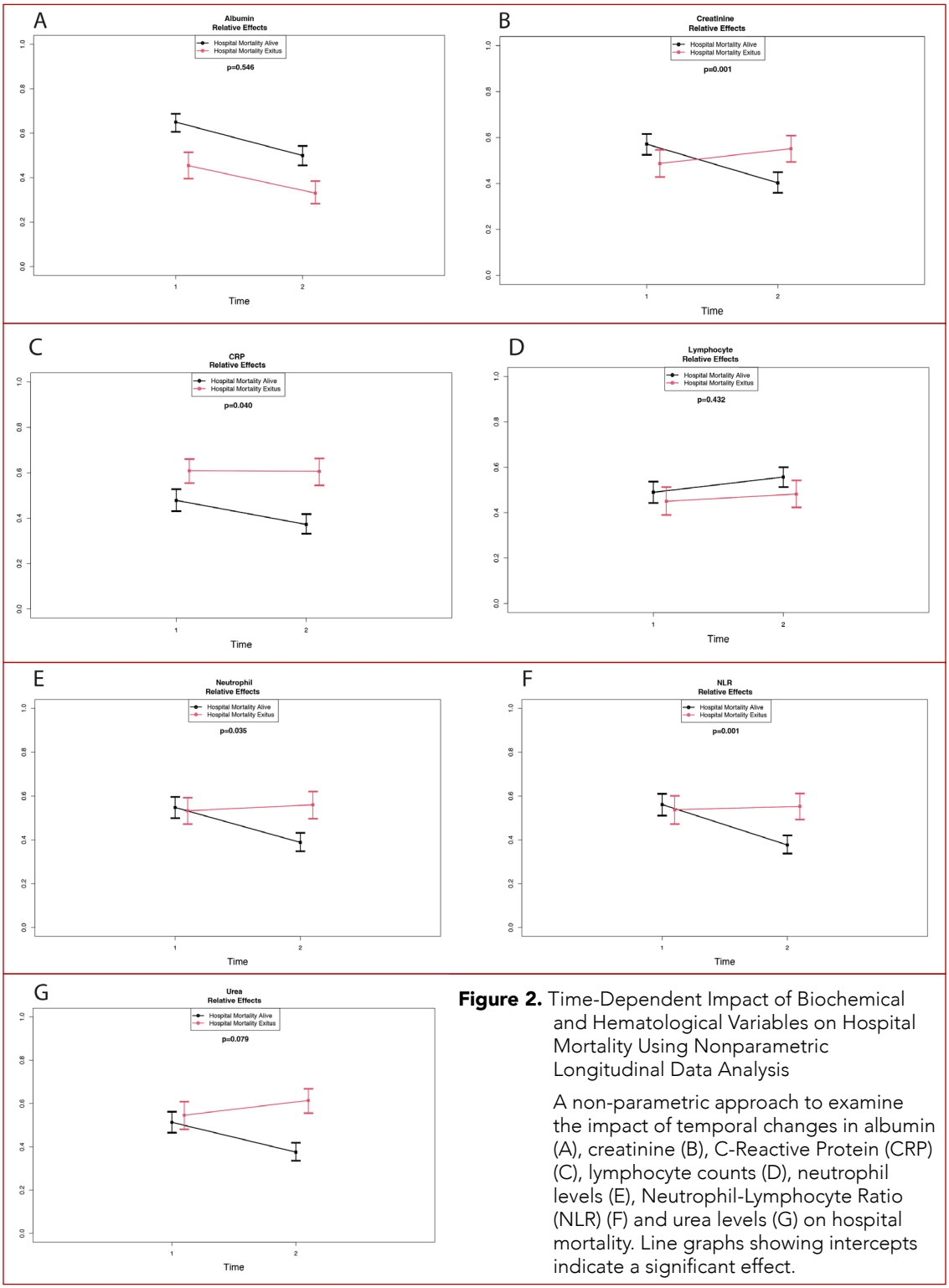

Figure 2. Time-Dependent Impact of Biochemical and Hematological Variables on Hospital Mortality Using Nonparametric Longitudinal Data Analysis

A non-parametric approach to examine the impact of temporal changes in albumin (A), creatinine (B), C-Reactive Protein (CRP) (C), lymphocyte counts (D), neutrophil levels (E), Neutrophil-Lymphocyte Ratio (NLR) (F) and urea levels (G) on hospital mortality. Line graphs showing intercepts indicate a significant effect.

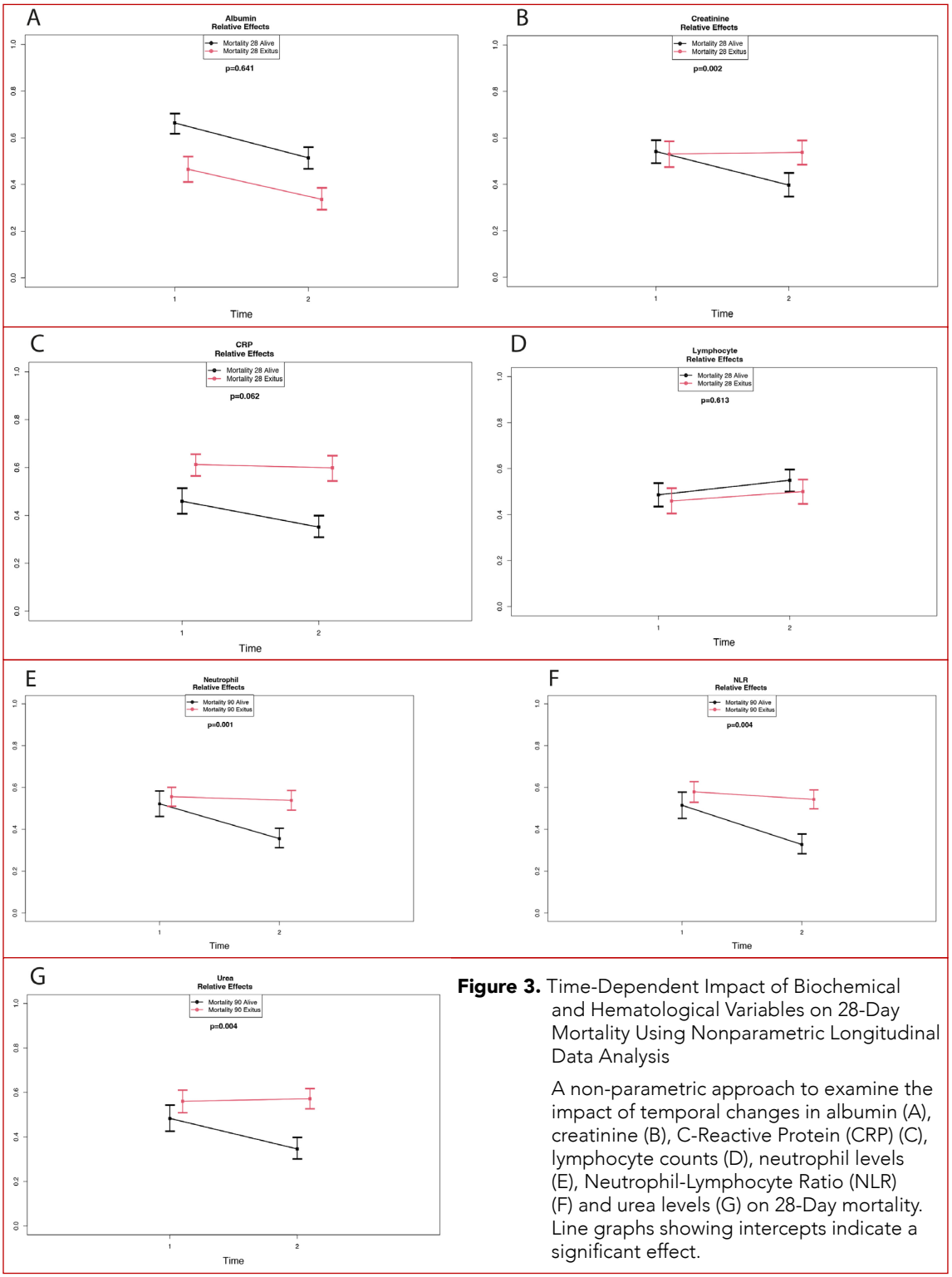

Figure 3. Time-Dependent Impact of Biochemical and Hematological Variables on 28-Day Mortality Using Nonparametric Longitudinal Data Analysis

A non-parametric approach to examine the impact of temporal changes in albumin (A), creatinine (B), C-Reactive Protein (CRP) (C), lymphocyte counts (D), neutrophil levels (E), Neutrophil-Lymphocyte Ratio (NLR) (F) and urea levels (G) on 28-Day mortality. Line graphs showing intercepts indicate a significant effect.

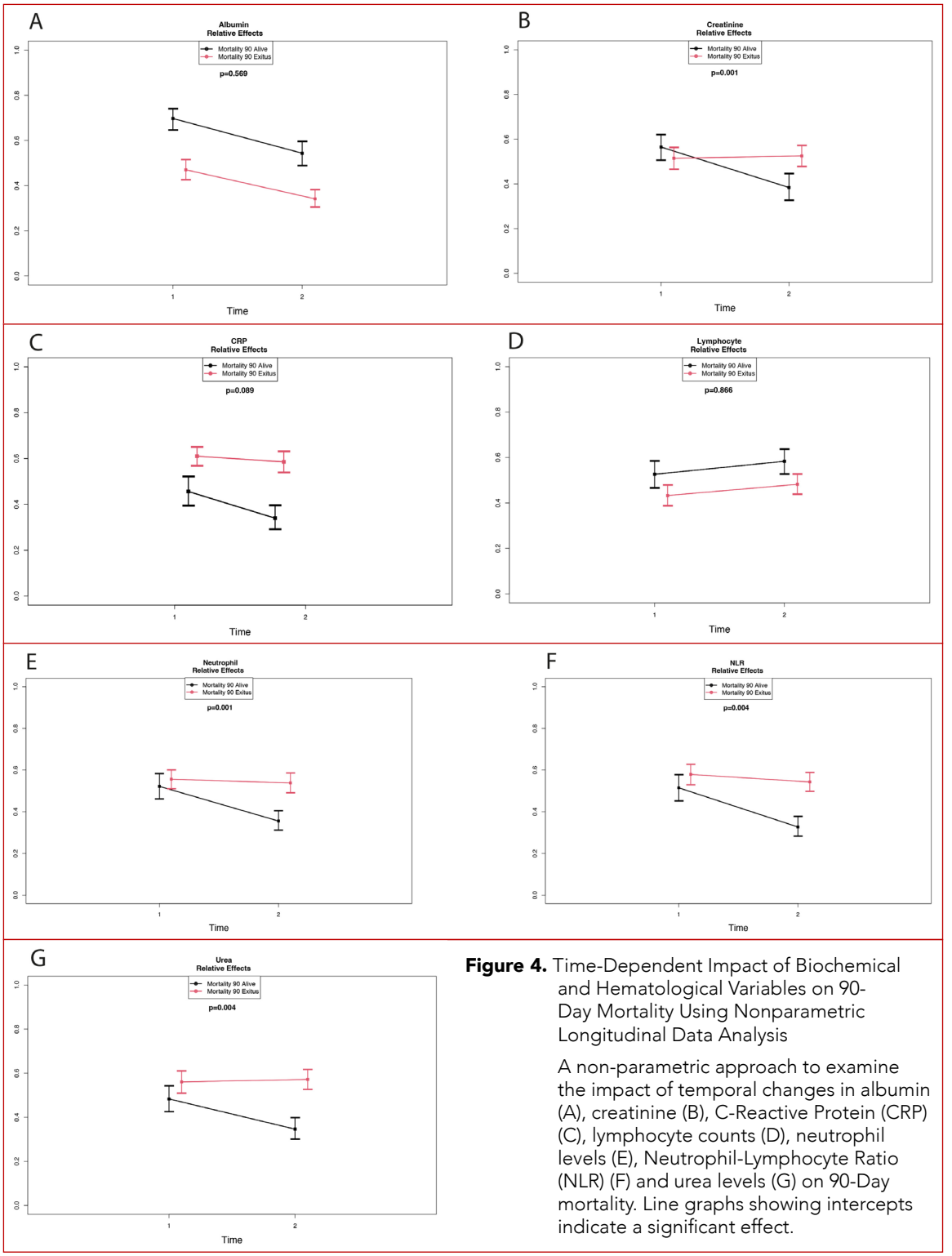

Figure 4. Time-Dependent Impact of Biochemical and Hematological Variables on 90-Day Mortality Using Nonparametric Longitudinal Data Analysis

A non-parametric approach to examine the impact of temporal changes in albumin (A), creatinine (B), C-Reactive Protein (CRP) (C), lymphocyte counts (D), neutrophil levels (E), Neutrophil-Lymphocyte Ratio (NLR) (F) and urea levels (G) on 90-Day mortality. Line graphs showing intercepts indicate a significant effect.

Trends in NT-proBNP, Mean Platelet Volume, and Systolic Blood Pressure Across Different Time Points

During hospitalization, NT-proBNP levels significantly decreased in survivors (p=0.017), while remaining stable in patients with mortality (p=0.683). These levels were notably higher in patients with mortality at the second measurement (p=0.024). Mean platelet volume showed a significant increase in patients who died (p=0.027). Systolic blood pressure significantly decreased in patients with mortality (p=0.009) and was notably lower at the second measurement compared to survivors (p=0.001) (Table 5).

At the 28-day mark, NT-proBNP levels again decreased significantly in survivors (p=0.013) but did not change in patients with mortality (p=0.625). At the second measurement, these levels were significantly higher in patients with mortality (p=0.005). Systolic blood pressure showed a significant decrease over time in patients who died (p=0.038), with lower levels at the second measurement compared to survivors (p=0.010) (Table 6).

At the 90-day follow-up, a significant decrease in NT-proBNP levels was observed in survivors (p=0.013), with no change in patients with mortality (p=0.616). At the second measurement, NT-proBNP levels were significantly higher in patients with mortality (p=0.006). Systolic blood pressure did not show a significant change in survivors but was significantly lower in patients with mortality at the second measurement (p=0.005) (Table 7).

Cox Regression Findings

Hospital Mortality: The univariate analysis revealed significant effects of AKI etiology, inotrope use, and levels of CRP (2) and NLR (2) on hospital mortality (p<0.05 for each). Specifically, sepsis was associated with a 2.4-fold increase in hospital mortality compared to cardiorenal syndrome, and inotrope use was linked to a 3.42-fold increase. A one-unit increase in CRP (2) and NLR (2) was found to elevate the risk of death by 3% and 1%, respectively. Multivariate analysis echoed these findings, showing that AKI etiology, inotrope use, and CRP (2) levels significantly influenced hospital mortality (p<0.05 for each), with sepsis raising mortality risk 2.59-fold compared to cardiorenal syndrome, and inotrope use increasing it by 1.96-fold. Additionally, each unit increase in CRP (2) upped hospital mortality risk by 4% (Table 8).

28-Day Mortality: In the univariate Cox model, AKI etiology, inotrope use, and levels of CRP (2), NLR (2), and creatinine (2) significantly affected 28-day mortality (p<0.05 for each). Sepsis resulted in a 2.8-fold increase in 28-day mortality compared to cardiorenal syndrome, and inotrope use led to a 3.01-fold increase. Increments of one unit in CRP (2), NLR (2), and creatinine (2) heightened the 28-day mortality risk by 3%, 1%, and 13%, respectively. The multivariate analysis indicated significant effects of AKI etiology, inotrope use, CRP (2), and creatinine (2) on 28-day mortality (p<0.05 for each). Sepsis increased the 28-day mortality risk by 1.99 times compared to cardiorenal syndrome, and inotrope use by 2.37 times. Moreover, each unit rise in CRP (2) and creatinine (2) increased the 28-day mortality risk by 4% and 1%, respectively (Table 9).

90-Day Mortality: The univariate analysis demonstrated significant impacts of AKI etiology, inotrope use, CRP (2), and NLR (2) levels on 90-day mortality (p<0.05 for each). Sepsis led to a 1.94-fold increase in 90-day mortality compared to cardiorenal syndrome, while nephrotoxic drug use showed a 90% reduction. Inotrope use was associated with a 2.64-fold increase in mortality. Increases of one unit in CRP (2) and NLR (2) raised the 90-day mortality risk by 3% and 1%, respectively. The multivariate analysis, including creatinine (2), revealed significant effects of AKI etiology, inotrope use, CRP (2), NLR (2), and creatinine(2) on 90-day mortality (p<0.05 for each). There was a 91% reduction in 90-day mortality in patients with nephrotoxic drug use compared to those with cardiorenal syndrome and

Table 5. Impact of Temporal Changes in Biochemical and Clinical Variables on in-hospital Mortality

	Hospital Mortality		p*
	Alive (n=85)	**Mortality** (n=59)	
NT-proBNP 1 §	16514.0 [347.9 – 70000.0]	9019.5 [924.0 – 95656.0]	0.873
NT-proBNP 2 §	3681.0 [704.0 – 70000.0]	18229.0 [330.0 – 70000.0]	**0.024**
p**	**0.017**	0.683	
Troponin 1 §	71.0 [0.0 – 4413.0]	110.5 [13.0 – 7590.0]	0.236
Troponin 2 §	59.5 [16.0 – 145.0]	161.0 [161.0 – 161.0]	0.286
p**	0.313	NaN	
Mean Platelet Volume 1 §	10.9 [7.9 – 13.7]	11.0 [7.9 – 13.1]	0.632
Mean Platelet Volume 2 §	11.0 [7.3 – 14.0]	11.4 [8.5 – 13.7]	0.164
p**	0.441	**0.027**	
Systolic Blood Pressure 1 §	110.0 [80.0 – 215.0]	113.0 [87.0 – 170.0]	0.818
Systolic blood pressure 2 §	128.0 [100.0 – 145.0]	86.0 [72.0 – 130.0]	**0.001**
p**	0.332	**0.009**	
Diastolic Blood Pressure 1 §	66.0 [43.0 – 95.0]	61.0 [48.0 – 95.0]	0.818
Diastolic Blood Pressure 2 §	69.0 [60.0 – 89.0]	53.0 [41.0 – 62.0]	**<0.001**
p**	0.187	**0.014**	
Mean Arterial Pressure 1 §	88.5 [60.0 – 125.0]	79.0 [61.0 – 116.0]	0.455
Mean Arterial Pressure 2 §	96.3 [76.0 – 111.0]	66.2 [51.0 – 73.0]	**<0.001**
p**	0.330	**0.014**	
Pulse Pressure 1 §	42.5 [30.0 – 148.0]	48.5 [32.0 – 120.0]	0.643
Pulse Pressure 2 §	51.0 [33.0 – 70.0]	32.0 [20.0 – 52.0]	**0.004**
p**	0.451	**0.050**	
Heart Rate 1 §	102.0 [72.0 – 143.0]	85.0 [61.0 – 110.0]	0.188
Heart Rate 2 §	92.0 [77.0 – 107.0]	95.5 [68.0 – 112.0]	0.949
p**	0.221	0.625	

Footnote: In Table 5, hospital mortality data are analyzed with a focus on various physiological and laboratory parameters. The § symbol indicates that values are presented as median with the range [Minimum-Maximum]. The table compares parameters between 'Alive' and 'Mortality' groups at two different time points: 1 represents values at admission, and 2 represents values at discharge or death. The statistical tests applied are signified as follows: The * symbol denotes the use of the Mann-Whitney U test, which is employed to assess differences in median values between two independent samples. The ** symbol indicates the use of the Wilcoxon test, which is utilized for paired comparisons to evaluate differences in repeated measurements or matched samples within the same group. These tests help in understanding the statistical significance of differences observed in clinical measures such as NT-proBNP, troponin, mean platelet volume, systolic and diastolic blood pressure, mean arterial pressure, pulse pressure, and heart rate across the two groups and at different time points in the study. The 'NaN' (Not a Number) value in the table under hospital mortality for Troponin 2 indicates that the data is not available or cannot be calculated.

Table 6. Impact of Temporal Changes in Biochemical and Clinical Variables on 28-Day Mortality

	Mortality 28		p*
	Alive (n=76)	**Mortality** (n=68)	
NT-proBNP 1 §	10479.0 [347.9 – 70000.0]	15223.0 [924.0 – 95656.0]	0.232
NT-proBNP 2 §	3302.5 [704.0 – 62515.0]	23869.0 [330.0 – 70000.0]	**0.005**
p**	0.**013**	0.625	
Troponin 1 §	62.0 [0.0 – 4413.0]	110.0 [13.0 – 7590.0]	0.093
Troponin 2 §	59.5 [16.0 – 145.0]	161.0 [161.0 – 161.0]	0.286
p**	0.313	NaN	
Mean Platelet Volume 1 §	11.0 [7.9 – 13.7]	10.9 [7.9 – 13.1]	0.891
Mean Platelet Volume 2 §	11.0 [7.3 – 14.0]	11.4 [8.5 – 13.7]	0.102
p**	0.753	**0.010**	
Systolic Blood Pressure 1 §	125.5 [80.0 – 215.0]	106.5 [87.0 – 170.0]	0.512
Systolic Blood pressure 2 §	125.0 [80.0 – 145.0]	93.0 [72.0 – 130.0]	**0.010**
p**	0.758	**0.038**	
Diastolic Blood Pressure 1 §	68.0 [43.0 – 95.0]	60.0 [48.0 – 90.0]	0.319
Diastolic Blood Pressure 2 §	68.0 [60.0 – 89.0]	53.0 [41.0 – 86.0]	**0.005**
p**	0.452	0.141	
Mean Arterial Pressure 1 §	90.0 [60.0 – 125.0]	77.7 [61.0 – 100.0]	0.161
Mean Arterial Pressure 2 §	93.5 [66.0 – 111.0]	66.3 [51.0 – 100.0]	**0.006**
p**	0.706	**0.041**	
Pulse Pressure 1 §	50.0 [30.0 – 148.0]	43.0 [32.0 – 120.0]	0.483
Pulse Pressure 2 §	51.0 [20.0 – 70.0]	36.5 [24.0 – 52.0]	**0.024**
p**	0.851	0.092	
Heart Rate 1 §	96.0 [61.0 – 143.0]	96.0 [81.0 – 110.0]	0.999
Heart Rate 2 §	90.0 [68.0 – 107.0]	96.0 [95.0 – 112.0]	0.295
p**	0.307	0.750	

Footnote: Table 6 focuses on the analysis of various clinical parameters and their association with 28-day mortality. The § symbol in the table represents that the values are given as median and range [Minimum-Maximum]. This table compares clinical measurements between the 'Alive' and 'Mortality' groups, specifically looking at changes from admission (1) to discharge or death (2). The * symbol indicates the use of the Mann-Whitney U test, which assesses differences in median values between two independent groups. The ** symbol denotes the application of the Wilcoxon test, used for paired comparisons to analyze differences in these parameters over time within the same group. Parameters such as NT-proBNP, troponin, mean platelet volume, systolic and diastolic blood pressure, mean arterial pressure, pulse pressure, and heart rate are evaluated to determine their significance in relation to mortality outcomes. The 'NaN' (Not a Number) value in the table under hospital mortality for Troponin 2 indicates that the data is not available or cannot be calculated.

Table 7. Impact of Temporal Changes in Biochemical and Clinical Variables on 90-Day Mortality

	Mortality 90		p*
	Alive (n=63)	**Mortality** (n=81)	
NT-proBNP 1 §	16514.0 [347.9 – 70000.0]	9710.0 [924.0 – 95656.0]	0.351
NT-proBNP 2 §	2589.0 [704.0 – 62515.0]	11367.0 [330.0 – 70000.0]	**0.006**
p**	**0.013**	0.616	
Troponin 1 §	56.5 [0.0 – 4413.0]	110.5 [13.0 – 7590.0]	**0.010**
Troponin 2 §	59.5 [16.0 – 145.0]	161.0 [161.0 – 161.0]	0.286
p**	0.313	NaN	
Mean Platelet Volume 1 §	10.9 [7.9 – 13.7]	11.0 [7.9 – 13.1]	0.745
Mean Platelet Volume 2 §	10.9 [7.3 – 14.0]	11.4 [8.5 – 13.7]	**0.010**
p**	0.805	**0.003**	
Systolic Blood Pressure 1 §	122.0 [83.0 – 215.0]	110.0 [80.0 – 170.0]	0.738
Systolic Blood pressure 2 §	128.0 [109.0 – 145.0]	100.0 [72.0 – 140.0]	**0.005**
p**	0.624	0.093	
Diastolic Blood Pressure 1 §	64.0 [43.0 – 95.0]	65.0 [48.0 – 95.0]	0.983
Diastolic Blood Pressure 2 §	68.0 [60.0 – 89.0]	60.0 [41.0 – 86.0]	**0.019**
p**	0.326	0.182	
Mean Arterial Pressure 1 §	88.0 [60.0 – 125.0]	80.3 [60.0 – 116.0]	0.363
Mean Arterial Pressure 2 §	96.0 [76.0 – 111.0]	66.3 [51.0 – 100.0]	**0.009**
p**	0.688	0.130	
Pulse Pressure 1 §	45.0 [34.0 – 148.0]	48.0 [30.0 – 120.0]	0.716
Pulse Pressure 2 §	51.0 [33.0 – 70.0]	33.0 [20.0 – 63.0]	**0.008**
p**	0.656	0.109	
Heart Rate 1 §	103.0 [72.0 – 143.0]	86.5 [61.0 – 110.0]	0.130
Heart Rate 2 §	94.5 [77.0 – 107.0]	95.0 [68.0 – 112.0]	0.953
p**	0.232	0.584	

Footnote: Table 7 presents data on 90-day mortality outcomes and their correlation with various clinical parameters. The § symbol indicates that the data are expressed as median values accompanied by their respective range [Minimum-Maximum]. This table compares clinical measurements, such as NT-proBNP and troponin levels, mean platelet volume, systolic and diastolic blood pressure, mean arterial pressure, pulse pressure, and heart rate, between the 'Alive' and 'Mortality' groups at two time points: '1' for values at admission and '2' for values at discharge or death. The statistical analysis is conducted using the * symbol, representing the Mann-Whitney U test, which is applied for assessing differences in median values between two independent groups. The ** symbol indicates the Wilcoxon test, which is used for paired comparisons, analyzing changes in these parameters over the course of the hospital stay within the same group. These analyses help in understanding the impact of these clinical parameters on mortality outcomes over a 90-day period. The 'NaN' (Not a Number) value in the table under hospital mortality for Troponin 2 indicates that the data is not available or cannot be calculated.

Table 8. Impact of Clinical Factors on Hospital Mortality Analyzed through Cox Proportional Hazards Model

Cox's proportional hazard model on time to event (Hospital Mortality)	Univariate		Multivariate	
	HR [95%CI]	p-value	HR [95%CI]	p-value
Acute Kidney Injury Etiology: *ref.=Cardiorenal Syndrome*				
Sepsis	2.40 [1.08 – 5.35]	**0.032**	2.59 [1.21 – 5.57]	**0.014**
Malignancy	1.49 [0.49 – 4.60]	0.481	2.18 [0.86 – 5.49]	0.099
Nephrotoxic Drugs	0.01 [0.01 – 0.02]	0.997	0.01 [0.01 – 0.02]	0.997
Other	0.92 [0.24 – 3.48]	0.904	2.11 [0.66 – 6.72]	0.205
Inotrope: Yes vs. No	3.42 [1.81 – 6.45]	**<0.001**	1.96 [1.10 – 3.50]	**0.022**
CRP 1	1.02 [0.99 – 1.06]	0.172		
CRP 2	1.03 [1.02 – 1.05]	**<0.001**	1.04 [1.02 – 1.06]	**<0.001**
NLR 1	1.01 [0.99 – 1.03]	0.246		
NLR 2	1.01 [1.01 – 1.02]	**0.029**	1.01 [0.99 – 1.02]	0.084
Creatinine 1	0.95 [0.84 – 1.07]	0.376		
Creatinine 2	1.11 [0.99 – 1.25]	0.059	1.07 [0.98 – 1.18]	0.134
MPV 1	1.02 [0.79 – 1.32]	0.862		
MPV 2	1.19 [0.92 – 1.52]	0.181		

Footnote: Table 8 presents the analysis of clinical factors on hospital mortality using the Cox Proportional Hazards Model. The model assesses the impact of factors such as Acute Kidney Injury (AKI) etiology, inotrope use, CRP, NLR, and creatinine levels on time to event (Hospital Mortality). Hazard Ratios (HR) with 95% Confidence Intervals (CI) are reported for both univariate and multivariate analyses, indicating the strength and direction of the association between each factor and hospital mortality. HRs greater than 1 indicate an increased risk of mortality. The 'ref.' denotes the reference category against which comparisons are made. P-values indicate the statistical significance of the associations, with values less than 0.05 considered significant.

Table 9. Impact of Clinical Factors on 28-Day Mortality Analyzed through Cox Proportional Hazards Model

Cox's proportional hazard model on time to event (Mortality 28)	HR [95%CI]		p-value	
	HR [95%CI]	p-value	HR [95%CI]	p-value
Acute Kidney Injury Etiology: *ref.=Cardiorenal Syndrome*				
Sepsis	2.80 [1.38 – 5.69]	**0.004**	1.99 [1.03 – 3.85]	**0.042**
Malignancy	1.47 [0.57 – 3.80]	0.422	1.67 [0.76 – 3.68]	0.201
Nephrotoxic Drugs	0.19 [0.02 – 1.47]	0.112	0.19 [0.02 – 1.45]	0.109
Other	1.39 [0.44 – 4.36]	0.575	2.51 [0.92 – 6.88]	0.073
Inotrope: Yes vs. No	3.01 [1.7 – 5.34]	**<0.001**	2.37 [1.36 – 4.13]	**0.002**
CRP 1	1.01 [0.99 – 1.04]	0.292	-	-
CRP 2	1.03 [1.01 – 1.05]	**<0.001**	1.04 [1.02 – 1.05]	**<0.001**
NLR 1	1.01 [0.98 – 1.02]	0.780	-	-
NLR 2	1.01 [1.01 – 1.02]	**0.022**	1.01 [0.99 – 1.02]	0.055
Creatinine 1	0.96 [0.87 – 1.06]	0.372	-	-
Creatinine 2	1.13 [1.01 – 1.26]	**0.030**	1.1 [1.01 – 1.21]	**0.031**
MPV 1	0.97 [0.76 – 1.25]	0.837	-	-
MPV 2	1.07 [0.85 – 1.35]	0.559	-	-

Footnote: In Table 9, the Cox Proportional Hazards Model is utilized to determine the impact of various clinical factors on 28-Day Mortality. This model provides insights into the risk factors influencing the likelihood of mortality within 28 days post-hospitalization. It includes variables such as AKI etiology, inotrope use, CRP, NLR, and creatinine levels. The table displays HRs and their respective 95% CIs, elucidating the proportional impact of each variable on 28-day mortality. Statistical significance is denoted by p-values, where a value below 0.05 indicates a statistically significant effect on mortality risk. The 'ref.' denotes the reference category against which comparisons are made.

Table 10. Impact of Clinical Factors on 90-Day Mortality Analyzed through Cox Proportional Hazards Model

Cox's proportional hazard model on time to event (Mortality 90)	HR [95%CI]		p-value	
	HR [95%CI]	p-value	HR [95%CI]	p-value
Acute Kidney Injury Etiology: *ref.=Cardiorenal Syndrome*				
Sepsis	1.94 [1.07 – 3.51]	**0.030**	1.32 [0.75 – 2.32]	0.333
Malignancy	1.17 [0.53 – 2.61]	0.694	1.22 [0.61 – 2.43]	0.572
Nephrotoxic Drugs	0.10 [0.01 – 0.78]	**0.027**	0.09 [0.01 – 0.67]	**0.019**
Other	0.8 [0.27 – 2.36]	0.683	1.32 [0.52 – 3.38]	0.556
Inotrope: Yes vs. No	2.64 [1.58 – 4.42]	**<0.001**	2.27 [1.37 – 3.76]	**0.002**
CRP 1	1.01 [0.99 – 1.04]	0.241	-	-
CRP 2	1.03 [1.02 – 1.05]	**<0.001**	1.03 [1.02 – 1.05]	**<0.001**
NLR 1	1.01 [0.99 – 1.02]	0.363	-	-
NLR 2	1.01 [1.01 – 1.02]	**0.017**	1.01 [1.01 – 1.02]	0.033
Creatinine 1	0.92 [0.84 – 1.02]	0.103	-	-
Creatinine 2	1.11 [0.99 – 1.23]	0.055	1.12 [1.03 – 1.22]	**0.010**
MPV 1	0.99 [0.79 – 1.23]	0.895	-	-
MPV 2	1.15 [0.93 – 1.42]	0.189	-	-

Footnote: Table 10 focuses on analyzing the effects of clinical factors on 90-Day Mortality through the Cox Proportional Hazards Model. This analysis is critical for understanding long-term outcomes post-hospitalization. The table includes variables like AKI etiology, inotrope usage, and biomarker levels (CRP, NLR, creatinine, MPV) and their respective hazard ratios, reflecting their influence on 90-day mortality risk. The HRs, along with 95% CIs, provide a quantitative measure of risk associated with each factor, with p-values highlighting the statistical significance of these relationships. Values below 0.05 p-value signify significant effects on mortality risk over a 90-day period. The 'ref.' denotes the reference category against which comparisons are made.

a 2.27-fold increase in patients requiring inotropes. A one-unit rise in CRP (2), NLR (2), and creatinine (2) enhanced the 90-day mortality risk by 3%, 1%, and 12%, respectively (Table 9).

DISCUSSION

This single-center retrospective cohort study describes the clinical characteristics, mortality, and factors associated with mortality in elderly patients who required acute hemodialysis during the course of AKI in the ICU. In-hospital mortality was 40.9% (n = 59), which is comparable to the results of other studies. In a retrospective analysis of 154 patients older than 80 years with AKI requiring dialysis, the overall mortality rate was 26.6% (13), but ICU patients were excluded. Other studies have reported mortality rates for elderly ICU patients with AKI of 63.5%–76.2% [11] and 53.1% (14). The highest mortality apart from these studies, reported by Chronopoulos et al., ranged from 31% to 80% (9). The definition of advanced age, treatment intensity, disease severity, and the unit in which the patient was followed have been suggested as reasons for the differing results (9). The lower in-hospital mortality in our study may be due to the inclusion of community-acquired AKI patients and the clinicians' experience in critical care management. The 28-day mortality was 47.2% (n = 68) and the 90-day mortality 56.2% (n = 81). The data are insufficient on the long-term outcomes of elderly people who develop AKI requiring hemodialysis. Coca reports that AKI is independently related to long-term mortality (10), and a prospective study including ICU patients determined that 66.7% of elderly patients with AKI progressing to dialysis treatment die within one year (15).

Comorbidities such as HT, DM, CAD, CKD, and HF have been reported as the most important risk factors for the development of AKI in elderly people (16). In a retrospective cohort study including 652 elderly patients, the most common comorbid

conditions were CVD (77.5%), HT (74.4%), and DM (35.8%) (17), but the same study observed no difference between survivors and non-survivors. Similarly, Santos et al. found no significant difference among comorbidities in terms of mortality (18); the most common comorbidities in their study were HT (80.5%), DM (43.7%), HF (40.2%), CVD (36.1%), and CKD (18.4%). Comorbidities were not associated with mortality.

The common causes of AKI in elderly ICU patients are hypotension of any cause (including hypovolemia and cardiac failure), sepsis, drug toxicity, obstructive causes, renal vascular disease, and glomerulonephritis. Sepsis has been reported to be involved in nearly half of all AKI cases (9, 17, 18). Duarte et al. found no difference in sepsis-related AKI mortality during hospitalization (13) when examining the relationship between etiology and mortality. Li et al. report that infections were significantly more frequent in the non-survival group at 90-day outcome (17). In a prospective observational study, the leading cause of etiology—sepsis—exhibited three times the death risk compared to pre-renal causes in the elderly (18). In our study, among etiologies, compared to cardiorenal syndrome, sepsis led to a 2.59-fold increase in in-hospital mortality and 1.99-fold increase in 28-day mortality.

Inotrope usage was significantly higher among non-survivors in in-hospital, 28-day and 90-day evaluations. Additionally, in univariate and multivariate analysis, mortality significantly increased in patients requiring inotropes for all three time periods. Our results are comparable with the current literature. Among 431 elderly patients with AKI, the use of vasopressors was associated with worse prognosis (19). Korula et al. (20) and Uchino et al. (1) also found the use of vasopressors to be associated with poor outcomes.

In recent studies, hypotension in AKI was associated with increased mortality (19, 21, 22). In the present study; among patients who required hemodialysis, we evaluated SBP across different time points and we found that SBP significantly decreased in patients with mortality. Considering that the leading etiology was sepsis, this may be related to the severity of the underlying disease. However, better perfusion of the kidney could be another reason, which warrants further investigation.

Regarding impact of temporal changes in laboratory parameters, laboratory parameter changes are notable findings of the current study. Additionally, in univariate and multivariate analysis, for all three time periods, we determined that increase in CRP indicated increased mortality. Among laboratory parameters, several factors are considered predictors of mortality in elderly patients with AKI. Serum albumin, CRP levels, and CRP/albumin ratio have been reported as mortality predictors in elderly patients with AKI requiring dialysis (13). Serum albumin, prealbumin, blood urea nitrogen levels, baseline estimated glomerular filtration rate, MAP, oliguria, and AKI severity were reported as 90-day mortality predictors in a retrospective study among 652 patients with AKI (17). Santos et al. report that mortality was significantly associated with an increase in urea and creatinine levels in elderly AKI patients (18). Although no distinction was made according to etiologies, the association of crp, a traditional marker, with mortality is not surprising and the demonstration of its temporal variation will guide the clinician in reviewing treatment options in practice.

The biochemical marker which we want to emphasize in detail is NT-proBNP. We found significant decrease in all three time periods among survivors. The prognostic significance of NT-proBNP has been demonstrated in HF (23). Moreover, NT-proBNP levels were associated with mortality in septic AKI patients receiving renal replacement therapy (24). Additionally, NT-proBNP and CRP were reported as independent predictors of mortality in sepsis patients older than 75 years of age (25). Although the present study includes heterogeneous etiology, our results reveals that in critical care

practice, NT-proBNP should be considered as a valuable marker for predicting mortality.

It is not surprising that critically ill elderly patients are susceptible to AKI, so age has drawn research interest, and advanced age has been independently associated with hospital mortality (1). Also, Bagshaw et al. observed a higher one-year mortality with advanced age (8), and older age has been identified as an independent risk factor for mortality in patients with AKI in the ICU (1, 26-28). Conversely, other studies did not find that increasing age had an impact on mortality (13, 17–19), nor did the present study identify age as a factor affecting mortality. Therefore, the survival of elderly patients with AKI in the ICU may be better than generally expected, and further studies should be considered to clarify the effect of age on mortality due to AKI. Finally, 16 of 93 surviving patients (17.2%) in our study were discharged on hemodialysis. Acuña et al. note that 18.9% of elderly patients with AKI progressed to dialysis treatment (15).

Although we presented highly selected patient group, it should be noted that our study has some limitations. First, it may not be appropriate to generalize our results, as this study had a retrospective design and was conducted at a single center. However, it may be considered as a pioneer for further research. In addition, the time from diagnosis of AKI to dialysis was not examined in our study, which may be considered another limitation. Finally, it was not possible to obtain long-term follow-up of renal function in patients who were discharged without dialysis, although we were able to report the number of patients on dialysis at discharge.

CONCLUSION

Elderly hospitalized patients have a significant rate of in-hospital death owing to AKI. Although advanced age exacerbates this situation, its effect on mortality may not be as expected. Therefore, chronological age should not be evaluated alone when deciding on dialysis in elderly patients. Appropriate laboratory parameters should be used as a guide in the decision-making process, and treatment intensity should be decided on a case-by-case basis. As this was a single-center retrospective study, the results cannot be generalized; future research is thus needed to obtain long-term follow-up of renal function in patients who were discharged without dialysis.

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Ethics approval and consent to participate:

The study was approved by the Ege University Ethics Committee, number 19-5.2T/69 and adhered to the principles of the Declaration of Helsinki. All patients or their relatives provided written informed consent.

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