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Original Article

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Frequency and Risk Factors of Early Mortality in Incident Hemodialysis Patients: A Retrospective Cohort Study

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ABSTRACT

Background: Early mortality remains a critical challenge among incident hemodialysis (HD) patients, particularly within the first 90 days of treatment. Identifying modifiable predictors of mortality during this vulnerable period is essential for improving patient outcomes.

Methods: This retrospective cohort study included 287 adult patients who initiated HD between January 2018 and December 2020. Demographic, clinical, and laboratory variables were analyzed to identify independent risk factors associated with all-cause mortality using multivariate logistic regression.

Results: Over a mean follow-up of 13.2 months, 87 patients (30%) died, with 10% of deaths occurring within the first 90 days. Cardiovascular disease and infections were the leading causes of death. In the multivariate analysis, independent predictors of mortality were malignancy (odds ratio [OR]: 7.82; 95% confidence interval [CI]: 3.11-19.66), cardiovascular disease (OR: 3.54; 95% CI: 1.64-6.00), heart failure (OR: 2.04; 95% CI: 1.27-3.29), and elevated C-reactive protein (CRP ≥ 5 mg/L) (OR: 2.89; 95% CI: 1.54-5.44). Although initiating HD with a tunneled catheter was more common among non-survivors, it was not an independent predictor in the adjusted model.

Conclusion: Early mortality in HD patients is strongly associated with systemic inflammation and cardiovascular burden. Malignancy, cardiovascular disease, heart failure, and elevated CRP levels emerged as significant independent predictors. These findings underscore the importance of early nephrology referral, inflammation control, and proactive vascular access planning. In addition to managing inflammation, early and systematic cardiovascular evaluation and malignancy screening may help further reduce early mortality in this high-risk population.

Keywords: Comorbidities, C-reactive protein, early mortality, hemodialysis, vascular access

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INTRODUCTION

Globally, hemodialysis (HD) is the most common form of kidney replacement therapy (KRT) for patients with kidney failure.[1] Although HD reduces morbidity and prolongs survival, adjusted all-cause mortality rates remain 6.5-7.9 times higher in HD patients compared to the general population.[2,3] The first year of dialysis is marked by particularly high mortality, with registry data from the United States, Canada, and Europe reporting early mortality rates ranging from 5.6% to 8.6% within the first 90 days and 16.2% to 24.3% during the first year of treatment.[4]

Several factors have been implicated in this increased mortality risk, including older age, low serum albumin, dysregulated phosphorus levels, anemia, and comorbidities such as diabetes and cardiovascular disease. Inflammation is increasingly recognized as a key contributor, with elevated inflammatory markers linked to poor outcomes.[5,6] Early nephrology referral and appropriate

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management of patients with chronic kidney disease (CKD) not treated with KRT have been associated with reduced early mortality.[7]

Among these, initiating HD with a central venous catheter is a well-known modifiable risk factor and is strongly associated with adverse outcomes.[8] However, late referral, unplanned dialysis initiation, and inadequate access planning remain prevalent in many regions.

A retrospective cohort from China found that the first 2 months after dialysis initiation were particularly critical, with age, female sex, diabetes, and hypertension as independent predictors.[9] Despite these international findings, data on early mortality and its risk factors among Turkish HD patients are scarce.

This study aimed to determine the period of highest mortality risk and identify independent predictors of early mortality among incident HD patients in a single tertiary center in Türkiye.

MATERIAL AND METHODS

A total of 310 patients were assessed for eligibility. Of these, 23 were excluded due to prior dialysis history, transfer to another center, discontinuation of dialysis, recovery of kidney function, or undergoing kidney transplantation. Thus, 287 patients were included in the final analysis. All patients were followed until death or until December 31, 2020, whichever came first. For patients who initiated HD in December 2020, follow-up continued until December 31, 2020, or death, whichever occurred first. The mean follow-up duration was 13.2 ± 7.5 months, with a total of 3176 patient-months observed. It is acknowledged that excluding patients who discontinued dialysis may introduce a competing risk; however, this was not statistically adjusted for and represents a limitation. As this was a retrospective study including all eligible patients during the study period, no formal power calculation was performed. Effect sizes and confidence intervals (CIs) are provided to support interpretation.

All included patients were followed until the end of 2020 or until the date of death. For patients who initiated HD in December 2020, follow-up continued until December 31, 2020, or death, whichever occurred first. All patients were receiving bicarbonate-buffered HD 3 times per week using synthetic hollow fiber polynephron membranes appropriate for their body surface area. Each session lasted 4 hours, with blood flow rates ranging from 250 to 350 mL/min (median: 300 mL/min).

Demographic and clinical data for all patients were obtained from HD file records, including age, sex, body mass index, duration of CKD before HD initiation, etiology of CKD, date of HD initiation, date of death, cause of death, initial vascular access type, comorbid conditions (e.g., diabetes mellitus, coronary artery disease, heart failure, atrial fibrillation, cerebrovascular disease, peripheral vascular disease, malignancy, chronic obstructive pulmonary disease [COPD]), smoking history, and the frequency and causes of hospitalizations.

Laboratory parameters were retrieved from the patients' records, including mean systolic and diastolic blood pressure, hemoglobin, white blood cell, platelet, and eosinophil counts, fasting blood glucose, blood urea nitrogen, creatinine, potassium, calcium, phosphorus, uric acid, albumin, total cholesterol, low-density lipoprotein, triglycerides, alanine aminotransferase, C-reactive protein (CRP), ferritin, parathyroid hormone, bicarbonate levels, and hepatitis markers. C-reactive protein levels were categorized as normal (<5 mg/L) or elevated (≥5 mg/L), based on laboratory reference ranges. The patients' volume status, average ultrafiltration volumes at the start of dialysis, and the number of hemodialysis sessions during the follow-up period were recorded from the HD medical records.

This study was conducted in accordance with the principles of the Declaration of Helsinki. The study protocol was reviewed and approved by the Başkent University Faculty of Medicine Ethics Committee (Approval No.: KA21/160 Date: 30.03.2021). The requirement for informed consent was waived due to the retrospective nature of the study, which utilized anonymized data from hospital records. The authors declare no conflicts of interest related to this study.

Given that the study period (January 2018 to December 2020) overlapped with the COVID-19 pandemic, the medical records of deceased patients were reviewed for documentation of COVID-19 infection.

Statistical Analysis

Statistical analyses were performed using SPSS version 25.0 (IBM SPSS Corp.; Armonk, NY, USA). Continuous variables were tested for normality using the Shapiro-Wilk test. Variables

MAIN POINTS

- Early mortality within the first 90 days of hemodialysis initiation remains high and is a critical concern in clinical nephrology practice.
- Malignancy, cardiovascular disease, heart failure, and elevated C-reactive protein (CRP ≥ 5 mg/L) levels were identified as independent predictors of early mortality in incident hemodialysis patients.
- Initiation of hemodialysis with a tunneled catheter was more common among non-survivors, suggesting a need for earlier nephrology referral and better vascular access planning.
- Systemic inflammation, as reflected by elevated CRP, plays a central role in early dialysis mortality and may serve as a target for early intervention.
- This study contributes national data from Türkiye and emphasizes the importance of multidisciplinary strategies, including early cardiovascular and malignancy evaluation, to improve early outcomes in hemodialysis patients.

following a normal distribution were presented as mean ± SD, while non-normally distributed variables were expressed as median (interquartile range, IQR). Categorical variables were summarized as frequencies and percentages. All variables with $P < .1$ in univariate analyses were considered for inclusion in the multivariate logistic regression model using a forward stepwise method.

Comparisons between groups (e.g., survivors vs. non-survivors) were performed using the independent samples t-test for normally distributed continuous variables and the Mann–Whitney *U* test for non-normally distributed continuous variables. Categorical variables were compared using the chi-square test or Fisher's exact test, as appropriate.

Univariate analyses were initially conducted to identify potential predictors of mortality, with statistical significance set at $P < .05$. Variables identified as significant in univariate analyses were included in a multivariate logistic regression model to determine independent risk factors for mortality. A stepwise forward selection method was employed to identify the most parsimonious model. Odds ratios (ORs) with 95% CIs were calculated to assess the strength of associations.

Kaplan–Meier survival curves were used to visualize mortality over time and compare groups using the log-rank test, as shown in Figure 1. Statistical significance was set at $P < .05$ for all analyses. Variables with missing data were excluded from multivariate analysis via case-wise deletion. The proportion of missing data did not exceed 5% for any variable.

RESULTS

Table 1 shows the demographic data of the patients. The most common underlying cause of CKD was diabetic nephropathy, observed in 41% of patients, followed by hypertensive nephrosclerosis in 14% and chronic glomerulonephritis in 14%. Regarding comorbidities, 53% of the patients had diabetes mellitus, 54% had documented cardiovascular disease (CVD), 24% had heart failure (HF), 8% had atrial fibrillation, 77% had hypertension, 11% had COPD, and 10% had malignancy.

During the follow-up period, death occurred in 87 patients (30%), with 10% of these deaths occurring within the first 3 months after the initiation of HD. The leading causes of death were CVD, accounting for 40 cases (17%), and infections, which were responsible for 24 cases (8%). Among the patients, 77% initiated HD using a tunneled central venous catheter as the first vascular access.

Table 2 summarizes the significant univariate associations between clinical variables and mortality. Non-survivors were significantly older than survivors (68.14 ± 12.41 vs. 59.65 ± 15.56 years, $P = .001$) and had a lower body mass index (24.78 ± 6.27 vs. 26.12 ± 5.12 kg/m^2, $P = .026$). Comorbidities such as CVD (76.7% vs. 45.3%, $P = .001$), heart failure (40.7% vs. 16.4%, $P = .001$), atrial fibrillation (16.3% vs. 4.0%, $P = .001$), COPD (17.4% vs. 8.0%, $P = .018$), and malignancy (22.1% vs. 5.0%, $P = .001$) were significantly more common in the deceased group. Smoking was also more prevalent among non-survivors (47.7% vs. 33.3%, $P = .022$). Laboratory findings showed that non-survivors had higher white blood cell counts (9.15 ± 3.62 vs. 8.16 ± 3.49 ×10^9/L, $P = .031$), more frequent CRP elevation (≥5 mg/L: 73.3% vs. 46.0%, $P = .001$), lower serum albumin levels (<4 g/dL: 78.6% vs. 52.3%, $P = .001$), and lower systolic and diastolic blood pressure (Sistolic blood pressure: 130.70 ± 21.23 vs. 144.23 ± 23.81 mm Hg, $P = .001$; Diastolic blood pressure: 75.41 ± 9.95 vs. 80.30 ± 11.34 mm Hg, $P = .001$). Median urine output was lower in non-survivors (127.8 mL vs. 150.9 mL, $P = .029$). Initiation of HD with a tunneled catheter was more common among non-survivors (85.5% vs. 72.5%, $P = .003$). Ferritin levels were also higher in non-survivors, though the difference was only marginally significant ($P = .040$). No statistically significant differences were found between survivors and non-survivors in terms of serum calcium, phosphorus, or parathyroid hormone levels.

Table 1. Baseline Demographic and Clinical Characteristics of Patients

Age (years)	**62 ± 15**
Gender, n (%)	
Male	151 (53)
Female	136 (47)
Body mass index (kg/m^2)	25 ± 5
History of hepatitis, n (%)	
Yes	27 (9)
No	260 (91)
Vascular access type, n (%)	
Central tunneled catheter	222 (77)
Arterio venous fistula	65(23)
Etiology, n (%)	
Diabetes mellitus	120 (41)
Hypertensive nephrosclerosis	40 (14)
Chronic glomerulonephritis	41 (14)
Ischemic nephrosclerosis	20 (7)
Chronic pyelonephritis	25 (9)
Genetic	11 (4)
Amyloidosis	6 (2)
Unknown	24 (8)
Comorbid diseases	
Diabetes mellitus	153 (53)
Cardiovascular disease	156 (54)
Heart failure	69 (24)
Atrial fibrillation	23 (8)
Hypertension	222 (77)
Chronic obstructive pulmonary disease	31 (11)
Malignancy	29 (10)
Smoking habit	179 (62)

Data are presented as mean ± standard deviation (SD) for continuous variables and as number (percentage) for categorical variables.

Table 2. Univariate Analysis of Factors Associated with Mortality

		Status		
		Survived	Deceased	*P*
Age (years)		59.65 ± 15.56	68.14 ± 12.41	**.001**
Body mass index (kg/m^2)		26.12 ± 5.12	24.78 ± 6.27	**.026**
Cardiovascular disease, n (%)	No	110 (54.7)	20 (23.3)	**.001**
	Yes	91 (45.3)	66 (76.7)	
Heart failure, n (%)	No	168 (83.6)	51 (59.3)	**.001**
	Yes	33 (16.4)	35 (40.7)	
Atrial fibrillation, n (%)	No	193 (96)	72 (83.7)	**.001**
	Yes	8 (4)	14 (16.3)	
Chronic obstructive pulmonary disease, n (%)	No	185 (92)	71 (82.6)	**.018**
	Yes	16 (8)	15 (17.4)	
Malignancy, n (%)	No	191 (95)	67 (77.9)	**.001**
	Yes	10 (5)	19 (22.1)	
Smoking habit, n (%)	No	134 (66.7)	45(52.3)	**.022**
	Yes	67 (33.3)	41 (47.7)	
White blood cell count		8.16 ± 3.49	9.15 ± 3.62	**.031**
C-reactive protein, n (%)	Normal	107 (54)	23 (26.7)	**.001**
	High	91 (46)	63 (73.3)	
Ferritin, n (%)	1	147 (73.1)	50 (58.1)	**.040**
	2	28 (13.9)	20 (23.3)	
	3	26 (12.9)	16 (18.6)	
Albumin (g/dL), n (%)	Low (<4 g/dL)	102 (52.3)	66 (78.6)	**.001**
	Normal (>4 g/dL)	93 (47.7)	18 (21.4)	
Systolic blood pressure (mm Hg)		144.23 ± 23.81	130.70 ± 21.23	**.001**
Diastolic blood pressure (mm Hg)		80.30 ± 11.34	75.41 ± 9.95	**.001**
Urine output (mL)		150.9 (10-3000)	127.8 (10-2000)	**.029**
Initiating HD with a catheter, n (%)		145 (72.5)	77 (85.5)	**.003**

HD, hemodialysis.

As shown in Table 3, 4 variables were independently associated with increased mortality risk in the multivariate logistic regression analysis. The presence of malignancy was the strongest predictor (OR: 7.82, 95% CI: 3.11-19.66, *P* = .001), followed by cardiovascular disease (OR: 3.54, 95% CI: 1.64-6.00, *P* = .001), heart failure (OR: 2.04, 95% CI: 1.27-3.29, *P* = .003), and elevated

Table 3. Multivariate Analysis of Independent Mortality Predictors

	B	SE	Wald	Exp (B) (Odds Ratio)	95 % CI (Lower-Upper)	*P*
Cardiovascular disease	1.142	0.331	11.932	3.535	1.639-5.997	**.001**
Heart failure	1.009	0.343	8.645	2.044	1.269-3.292	**.003**
Malignancy	2.057	0.471	19.122	7.824	3.113-19.656	**.001**
Elevated C-reactive protein	1.062	0.322	10.865	2.893	1.537-5.444	**.001**

B, regression coefficient (beta); CI, confidence interval; Exp B, exponentiated B; SE, standard error.

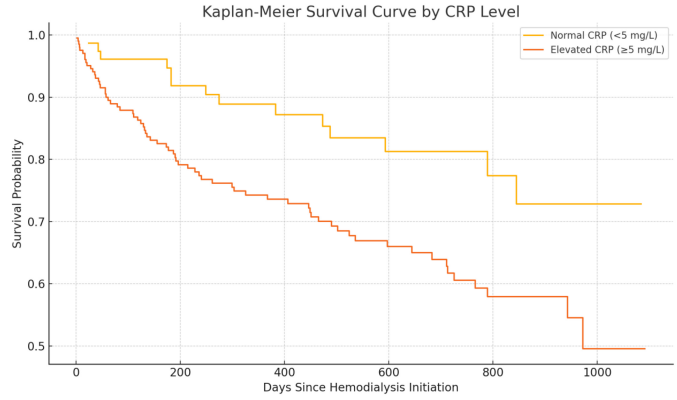

Figure 1. Kaplan–Meier survival curve by C-reactive protein (CRP) level. *Kaplan–Meier survival curves for patients stratified by CRP level. Patients with elevated CRP (≥5 mg/L) had significantly lower survival compared to those with normal CRP levels (<5 mg/L) (log-rank $P < .001$).

C-reactive protein levels (CRP ≥ 5 mg/L) (OR: 2.89, 95% CI: 1.54-5.44, $P = .001$).

Kaplan-Meier survival curves were constructed to evaluate mortality over time. Patients with elevated CRP levels exhibited significantly reduced survival probability compared to those with normal CRP levels (log-rank $P < .001$). Figure 1 illustrates the cumulative survival by CRP status.

DISCUSSION

This study provides valuable insights into early mortality among incident HD patients in the center. To our' knowledge, it is among the few studies focusing on early mortality in Turkish HD patients, a group underrepresented in international literature. In addition, Erdem et al[10] conducted a regional study in the Black Sea area of Türkiye, identifying similar comorbid risk factors such as advanced age and cardiovascular disease as predictors of long-term mortality among incident HD patients. Their findings are consistent with ours, supporting the relevance of cardiovascular burden across different Turkish populations.[10] These findings confirm that early mortality remains a major concern, particularly within the first 3 months after HD initiation, during which a 10% mortality rate was observed. This is consistent with data from international registries, including those from the United States, Canada, and Europe, which report 90-day mortality rates ranging from 5.6% to 8.6% and 1-year mortality rates between 16.2% and 24.3%.[4] The Dialysis Outcomes and Practice Patterns Study (DOPPS) similarly identified a mortality peak during the first month of HD, with rates up to 29.3 deaths per 100 patient-years.[11]

Only advanced age, CVD, HF, malignancy, and elevated CRP levels were all significantly associated with increased mortality. Among the 87 patients who died, none were recorded as having a confirmed COVID-19 diagnosis at the time of death. Therefore, mortality in this cohort cannot be directly attributed to COVID-19. In the multivariate analysis, the strongest independent predictors were malignancy (OR: 7.82), CVD (OR: 3.53), HF (OR: 2.04), and CRP ≥5 mg/L (OR: 2.89). These findings highlight the prominent role of systemic inflammation in early HD outcomes. Inflammation is a known contributor to vascular calcification, malnutrition-inflammation complex syndrome, and immune dysfunction—all of which can exacerbate mortality risk.[12]

Our findings are consistent with those from the multinational Peridialysis study, which demonstrated that suboptimal dialysis initiation (characterized by late nephrology referral, unplanned starts, or use of temporary access) was independently associated with increased first-year mortality.[13] In this study, 77% of patients started HD with a tunneled central venous catheter—a rate indicative of widespread unplanned dialysis initiation. Although catheter use did not remain statistically significant in multivariate analysis, its higher prevalence among non-survivors suggests that it may reflect late presentation and suboptimal care in patients with CKD not receiving KRT.

The prognostic value of systemic inflammation is further emphasized by the significant association between elevated CRP levels and mortality. While the threshold for elevated CRP was ≥5 mg/L, similar findings have been reported using different cutoffs in other cohorts, including the Peridialysis study.[12] Hypoalbuminemia—though not independently significant in multivariate analysis in the study—was also more prevalent among non-survivors and reflects the combined burden of inflammation and malnutrition. Though hyperphosphatemia did not reach significance in the analysis, it remains a recognized mortality risk factor in other studies and warrants close monitoring.

The Peridialysis study also identified a paradoxical association between higher estimated glomerular filtration rate at HD initiation and mortality, suggesting that early initiation based on biochemical criteria alone may not be beneficial in patients with high comorbidity or cachexia. This observation supports individualized decision-making and emphasizes the importance of clinical context over laboratory thresholds alone. The same study found no significant difference in first-year mortality between patients who selected peritoneal dialysis versus hemodialysis, highlighting the need for comprehensive education for patients with CKD not receiving KRT, and for shared decision-making.

International data support the consistency of these risk factors across healthcare settings. For instance, a multicenter Ethiopian study reported high early mortality despite a younger patient population, likely due to limited access to care and a high prevalence of catheter use. Infections were a major cause of death in both that cohort and ours, pointing again to the role of systemic inflammation and the complications of central venous catheters.[14] Cardiovascular disease was a dominant comorbidity in both populations, underlining its central role in early mortality.

This cohort exhibited high rates of diabetes mellitus (53%) and hypertension (77%), higher than those reported in international registries such as DOPPS.[10] Although neither diabetes nor hypertension emerged as independent predictors of mortality in the multivariate analysis, their contribution to the overall cardiovascular burden remains clinically important and may act through intermediary conditions such as heart failure or vascular disease. This underscores the importance of aggressive management of these comorbidities in the early dialysis period.

Previous large-scale studies further support the findings. For example, a Brazilian cohort of over 5000 incident HD patients identified older age, diabetes, unplanned dialysis initiation, and central venous catheter use as significant predictors of early mortality.[15] While the analysis did not find diabetes to be an independent risk factor, it remains an important contributor to the comorbidity burden, especially in resource-limited or delayed-referral settings.

The association between vascular access type and mortality is well established. A systematic review by Al-Jaishi et al[16] reported significantly higher all-cause and infection-related mortality among patients who started HD with catheters compared to those with arteriovenous fistulas, particularly during the first year of treatment. Although catheter use did not retain significance in the adjusted model, its frequent occurrence—especially among non-survivors—supports the notion that improving vascular access planning is a critical and modifiable component of early HD care.

This study has several limitations. Its retrospective, single-center design limits the generalizability of the findings. Patients who discontinued dialysis or were transferred to other centers were excluded, which may have introduced selection bias. Furthermore, key variables such as dialysis adequacy (Kt/V), standardized comorbidity indices (e.g., Charlson Index), medication adherence, and socioeconomic status were not assessed, although they are known to influence mortality outcomes.

Although hypoalbuminemia and systolic blood pressure were statistically significant in univariate analyses, they did not remain in the multivariate model—possibly due to multicollinearity or limited statistical power.

Another important limitation is the absence of standardized dialysis adequacy data. Because of the retrospective design, Kt/V values were inconsistently recorded and could not be included in the final analysis. Future prospective studies should incorporate uniform adequacy measures such as Kt/V to better assess their contribution to early mortality.

In addition, no formal sample size or power analysis (e.g., via G*Power) was performed prior to the study. The sample size was determined by the total number of eligible patients within the study period. While this reflects real-world clinical practice, it may have limited the ability to detect associations with smaller effect sizes.

Early mortality in HD patients is driven by a combination of systemic inflammation, cardiovascular burden, and late or suboptimal dialysis initiation. Independent predictors of early mortality in this cohort included malignancy, CVD, HF, and elevated CRP levels. Although catheter use was not independently associated with mortality after adjustment, its high prevalence among non-survivors and strong biological plausibility suggest it is a relevant surrogate marker for suboptimal care. Multidisciplinary efforts to promote early nephrology referral, optimize vascular access, and manage inflammation and comorbidities are essential to improve outcomes. In addition to managing inflammation, early and systematic cardiovascular assessment and malignancy screening may represent key strategies to further reduce early mortality in this high-risk population. Future multicenter, prospective studies with broader datasets are needed to validate these findings and guide intervention strategies.

Data Availability Statement: The data that support the findings of this study are available on request from the corresponding author.

Ethics Committee Approval: Ethical committee approval was received from the Ethics Committee of Başkent University (Approval No.: KA21/160; Date: 30.3.2021).

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