Factors Affecting Survival In Patients Undergoing Hemodialysis

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ABSTRACT

The article examines how age, gender, and several biochemical parameters affect survival to varying degrees in patients undergoing hemodialysis. The results indicate that a number of clinical and demographic factors have a significant negative impact on patient survival. It was found that for every 10-year increase in age, the risk of death rises by 1.61 times, demonstrating a significantly lower survival rate in elderly patients. The 28% higher risk of death in men compared to women is attributed to the higher prevalence of cardiovascular diseases among men. The presence of diabetes mellitus was found to nearly double the risk of death, and in hemodialysis patients, this disease was identified as an independent unfavorable prognostic factor. Chronic heart failure was determined to increase the risk of death by 2.5 times, making it one of the strongest negative factors among those analyzed.

Keywords: hemodialysis, chronic kidney disease, fibroblast-23, parathyroid hormone, vitamin D, viability.

Introduction. According to the International Society of Nephrologists and the Global Atlas of Kidney Health (ISN-GKHA), in 2023, 850 million people, i.e., about 10% of the world's population, were diagnosed with chronic kidney disease (CKD). Globally, the mortality rate from CKD is 2.4% of the average total mortality [1,2]. In practice, CKD is classified according to the classification recommended by the National Kidney Fund of the United States (USA) in 2002. According to it, 5 stages of this severe complication are distinguished [18].

Studies show that 25% of patients with CKD have limited knowledge about their health. This particularly negatively affects the health of people in lower socio-economic groups and leads to adverse clinical conditions [16]. Therefore, one of the main approaches to reducing the negative consequences of CKD is to increase public awareness and literacy about this disease, as well as ensure timely referral to a nephrologist and initiation of treatment in early stages [17].

The latter is very important, as CKD often progresses without symptoms and becomes clinically apparent only after a significant portion of glomerular function has been lost [13]. As it progresses from its early stages to severe renal failure, with glomerular filtration rate (GFR <15 ml/min per 1.73 m2 of body surface area), the costs of treatment and

mortality rates increase sharply without timely renal replacement therapy (hemodialysis), while life expectancy decreases significantly [10].

According to 2020 data, 3.9 million patients with CKD received hemodialysis, and although approximately the same number needed it, renal replacement procedures were not performed for various reasons [19].

In our study, we examined the influence of a number of external factors, as well as internal factors, i.e., certain laboratory changes, including fibroblast growth factor-23, on the survival of patients undergoing hemodialysis.

The elevation of FGF-23 in the blood begins at stage 2 CKD, even before changes in calcium, phosphorus, and parathyroid hormone levels are observed [21]. In the terminal stage, this protein indicator often exceeds the normal level by 100 to 1000 times [15]. There may be an inverse relationship between vitamin D, FGF-23, and mineral metabolism in blood serum. FGF-23 is both a cause and a consequence of abnormal changes in calcium and phosphates in blood serum [12].

An increase in parathyroid hormone (PTH) in the blood, parallel to the decrease in kidney function, is often one of the early detectable changes. Mortality from cardiovascular diseases is higher in patients with elevated levels of this hormone. According to statistical data provided by Chen et al., in a study of 958 elderly individuals, elevated levels of PTH in blood serum increased the risk of death from cardiovascular diseases by 37-38% [4].

The relationship between PTH and mortality from cardiovascular diseases can be explained by several mechanisms. First and foremost, this hormone directly participates in the processes of atherogenesis through vascular calcification and remodeling [6]. Additionally, PTH negatively affects the heart by causing left ventricular hypertrophy, calcification, and fibrosis [5].

In patients on hemodialysis, a significant correlation was found between serum FGF-23 levels and moderate to high left ventricular myocardial mass and low ejection fraction, independent of β-type natriuretic peptide and cardiac T-troponins [15].

Although some clinical observations suggest that FGF-23 is associated with an increase in C-reactive protein in CKD, there is insufficient data on its direct inducing effect on endothelial dysfunction [18].

The levels of FGF-23 during hemodialysis and the degree of its relationship with phosphorus have not been studied dynamically. Studying the blood parameters of this protein allows for the assessment of the microelement's significance in this group of patients.

It is known that the survival of patients receiving hemodialysis is influenced by numerous factors, particularly age, sex, stage of the disease, and various biochemical indicators to varying degrees. From this perspective, studying the relationship between each of these factors individually and their combined effect on survival indicators is of great practical importance. Taking this into account, we investigated the factors influencing patient survival.

Research materials and methods: The study involved 180 patients receiving hemodialysis in the terminal stage of chronic kidney disease in Samarkand region. Their average age was 50.4±5.52 years, comprising 112 men and 68 women. All patients were placed under comprehensive observation, with their medical history, comorbidities, and hemodialysis regimen being studied. They underwent general blood and urine analyses, as well as biochemical tests (including urea, creatinine, albumin, and several other indicators, along with vitamin D, parathyroid hormone, and fibroblast growth factor-23).

Based on the studied and obtained results, we assessed the factors influencing the survival of patients receiving hemodialysis in our observation using univariate logistic regression analysis. The obtained results are presented in Table 1.

Table 1.

Logistic regression analysis of factors influencing the survival of patients receiving hemodialysis

Variables	OR (odds ratio)	95% CI (Confidence interval)	P (Reliability)
Age, years	1.61	1.36-1.87	0.001
Sex, male	1.28	1.1-1.56	0.042
Diabetes	1.92	1.53-2.42	0.001
Chronic heart failure	2.54	1.95-3.24	0.001
Hypertension	1.62	1.38-1.90	0.001
Ischemic heart disease	1.50	1.22-1.90	0.001
Body Mass Index (BMI), kg/cm^2	1.70	1.30-2.20	0.001
Dialysis time duration, 4 hours	0.65	0.52-0.82	0.001
Central venous catheter	3.0	2.38-3.90	0.001
Arterio-venous fistula	1.52	1.20-2.0	0.003
Dialysis hypotension	2.0	1.55-2.6	0.001
Skipping a dialysis session	2.5	1.95-3.25	0.001
Hemoglobin, g/l	1.60	1.25-2.05	0.001
Albumin, g/l	0.84	0.70-0.94	0.001
Phosphorus, mmol/l	1.25	1.12-1.40	0.001
Parathyroid hormone, ng/ml	1.15	1.10-1.28	0.001
Fibroblast-23, ng/ml	1.68	1.40-2.0	0.001

C-reactive protein, mmol/l	1.15	1.12-1.24	0.001
Diuresis 200. ml/day	0.55	0.44-0.80	0.001

As shown in the table, for every 10-year increase in patient age, the risk of death increases by 1.61 times (OR = 1.61, 95% CI 1.36-1.87, p = 0.001), indicating lower survival rates in older patients. The risk of death in male patients was found to be 28% higher than in females (OR = 1.28, 95% CI 1.1-1.56, p = 0.042). This is closely linked to the higher prevalence of cardiovascular diseases in men.

In patients with diabetes mellitus, the risk of death was nearly 2 times higher (OR = 1.92, 95% CI 1.53-2.42, p=0.001). This can be considered the main independent factor for this disease in patients receiving hemodialysis. It was found that the risk of death in patients with chronic heart failure is 2.5 times higher compared to other patients (OR = 2.54, 95% CI 1.95-3.24, p = 0.001). This is considered one of the strongest negative influencing factors. It was noted that hypertension (OR = 1.62, 95% CI 1.38-1.90, p = 0.001) and coronary heart disease (OR = 1.50, 95% CI 11.22-1.90, p = 0.001) also had a significant negative impact on patient survival.

Our findings on the increased risk of death with age correspond to the results of large international studies. Specifically, the Dialysis Outcomes and Practice Patterns Study (DOPPS), a multicenter observational study, found that a 10-year increase in age is associated with a 15-20% increase in mortality risk [24]. This is attributed not only to biological aging but also to the co-occurrence of additional diseases (coronary heart disease, heart failure, rhythm disturbances, as well as a decrease in the body's adaptive capabilities). Therefore, it is advisable to consider age not as a separate prognostic factor, but as a comprehensive indicator of the patient's overall physical condition.

Laboratory analyses showed that higher albumin levels positively affect patient survival (OR = 0.84, 95% CI 0.70-0.94, p = 0.001). It was found that both very low and very high body mass index (OR = 1.70, 95% CI 1.30-2.20, p = 0.001) negatively affect the survival of patients receiving hemodialysis. Scientific literature provides reliable evidence that hypoalbuminemia in dialysis patients is not only a sign of nutritional deficiency but also an indicator of systemic inflammation. According to the results of a meta-analysis conducted by Kalantar-Zadeh et al., an increase in albumin levels by 1 g/l reduces the risk of death by 3-4%, and our results are consistent with these findings [8].

A high level of phosphorus (OR = 1.25, 95% CI 1.12-1.40, p = 0.001), parathyroid hormone (OR = 1.15, 95% CI 1.10-1.28, p = 0.001), and fibroblast-23 (OR = 1.68, 95% CI 1.40-2.0, p = 0.001), which play a key role in the body's mineral metabolism, negatively affects the state of blood vessels. According to KDIGO (2020), an increase in the indicators of the above-mentioned markers is the main factor in the development of vascular calcification [11]. In some studies, it was found that an increase in the level of fibroblast-23, regardless of the amount of phosphorus, is an independent predictor of mortality in patients on hemodialysis [7]. This once again confirms the important clinical significance of early detection of mineral-bone disorders.

It was established that a low hemoglobin level reduces the body's oxygen supply by 1.6 times (OR = 1.60, 95% CI 1.25-2.05, p = 0.001), which stimulates the intensification of systemic oxidation processes. It was confirmed that a high level of C-reactive protein also increases the risk of death in this group of patients (OR = 1.15, 95% CI 11.12-1.24, p = 0.001).

It is known that the duration of dialysis time in patients is 4 hours or more, which is a

protective factor and has a positive effect on survival. The results we obtained also confirmed this opinion (OR = 0.65, 95% CI 0.52-0.82, p=0.001).

It was also established that the use of a central venous catheter in patients undergoing dialysis increases the risk of sepsis and thrombosis in them by 200% (OR = 3.0, 95% CI 2.38-3.90, p=0.001). The frequency of these complications in patients with arteriovenous fistulas is 2 times lower than in patients with central catheterization (OR = 1.52, 95% CI 1.20-2.0, p=0.003). It was confirmed that in some patients, a decrease in arterial blood pressure during dialysis also negatively affects their survival (OR = 2.0, 95% CI 1.55-2.6, p=0.001). It was established that a daily independent diuresis of 200 ml or more in patients is also a protective factor (OR = 0.55, 95% CI 0.44-0.80, p=0.001). This situation had a positive impact on the quality of life. It was noted that missing a dialysis session is one of the most pronounced risk factors (OR = 2.5, 95% CI 1.95-3.25, p=0.001).

Using the above results, we conducted a ROC analysis to determine the combined sensitivity (Sensitivity) and specificity (Specificity) of all the studied factors affecting survival in patients undergoing hemodialysis, as well as their role in life expectancy prediction, which is presented in Figure 1.

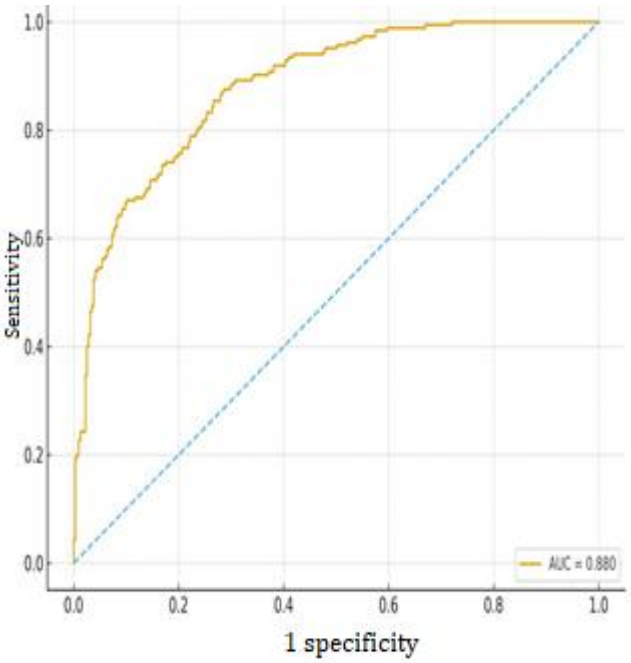


Figure 1. Joint ROC analysis of all factors influencing the survival of patients receiving hemodialysis.

As shown in the figure, based on the results of multifactorial ROC analysis, it was established that the combination of the studied indicators has a highly significant negative effect on patient survival (AUC=0.880, p<0.001).

However, during our observation, it was noted that not all the studied indicators were observed in each patient. Taking these circumstances into account, the ROC analysis was studied within the framework of the influence of age, sex, concomitant diseases, time of dialysis, and other similar factors on patient survival, which are presented in Figure 2 below.

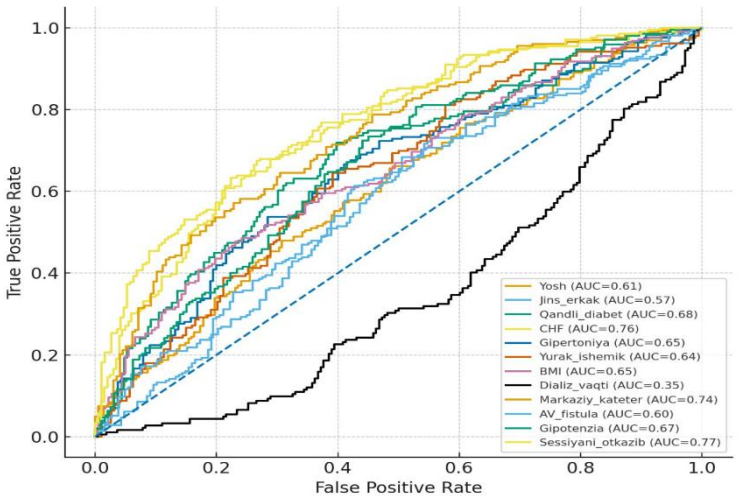
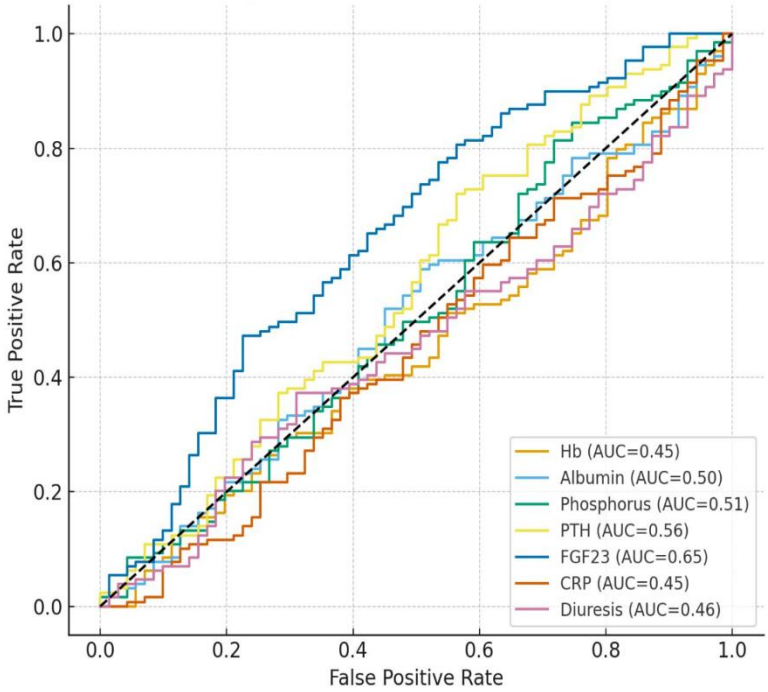


Figure 2. ROC curve of individual factors influencing the survival of patients receiving hemodialysis.

As shown in the figure, missing dialysis sessions (AUC=0.77), chronic heart failure (AUC=0.76), and central venous catheter use (AUC=0.74) were identified as factors with the strongest negative impact (p<0.001). Diabetes mellitus, arterial hypertension, coronary heart disease, body mass index (BMI), patient age, and arteriovenous fistula were determined to be moderate prognostic factors (p<0.05). Therefore, it is advisable for doctors to

carefully monitor these factors in patients undergoing hemodialysis procedures and address any modifiable risks when possible. This approach can positively affect patients' life expectancy. It was confirmed that the duration of dialysis time (AUC=0.35) had the opposite effect and acted as a protective factor. Similar findings to our results have also been reported by several other authors [14, 23, 3, 9].



In addition to the above, the ROC curve of each of the biochemical parameters affecting the survival of patients on hemodialysis was studied separately. The obtained results are presented in Figure 3.

Figure 3. ROC analysis of biochemical factors influencing the survival of patients receiving hemodialysis.

As shown in the figure, fibroblast-23 (AUC=0.65) was found to be a reliable ($p<0.05$) prognostic factor compared to other laboratory indicators. Albumin (AUC=0.50), C-reactive protein (AUC=0.45), hemoglobin (AUC=0.45), parathyroid hormone (AUC=0.56), phosphorus (AUC=0.51), and daily urine output (AUC=0.46) were noted to be weak prognostic factors.

Additionally, our results were similar to those obtained earlier by Gao and colleagues. They analyzed the relationship between FGF-23 levels and overall mortality and cardiovascular outcomes among patients receiving hemodialysis. According to their results: in the group with high FGF-23 levels, the odds ratio was ≈ 1.14 (95% confidence interval: 1.01-1.30, p=0.04), indicating a statistically significant association [21]. Another study demonstrated that in patients undergoing hemodialysis, high fibroblast-23 levels and low klotho protein in blood plasma negatively affected patient survival and quality of life [25]. The obtained results confirm that fibroblast-23 has a significant negative impact on patient survival and can be used to predict disease progression and determine the effectiveness of treatments in patients undergoing hemodialysis.

Conclusion. The results obtained showed that several clinical and demographic factors have a significant negative impact on patient survival. It was determined that for every 10-year increase in age, the risk of death rises by 1.61 times, confirming that survival rates in elderly patients are considerably lower. The 28% higher risk of death in men compared to women is attributed to the higher prevalence of cardiovascular diseases among men. The presence of diabetes mellitus was found to nearly double the risk of death, and in patients undergoing hemodialysis, this disease was identified as an independent negative prognostic factor. Chronic heart failure was found to increase the risk of death by 2.5 times, making it one of the strongest negative factors among the analyzed indicators. Additionally, arterial hypertension and coronary heart disease were noted to have a significant negative impact on patient survival. Overall, age, sex, diabetes mellitus, chronic heart failure, arterial hypertension, and coronary heart disease are considered the main independent factors increasing the risk of death in patients undergoing hemodialysis. Early detection and comprehensive management of these factors are crucial for improving patient survival. High serum albumin levels serve as a protective factor, reducing the risk of death, which indicates that hypoalbuminemia should be

assessed not only as a protein-energy deficiency but also as an indicator of systemic inflammation. Elevated levels of phosphorus, parathyroid hormone, and fibroblast growth factor-23 are important factors that increase the risk of death by enhancing calcium and cholesterol deposition in blood vessel walls. Low hemoglobin levels and increased C-reactive protein exacerbate systemic inflammation and hypoxia, negatively affecting patients' lives. Dialysis sessions lasting 4 hours or more, as well as the presence of preserved daily diuresis, improve survival as protective factors. Conversely, the use of central venous catheters, arterial hypotension during dialysis, and missing dialysis sessions are strong negative factors that sharply increase the risk of death. Early identification and timely management of these factors are important for increasing survival rates in patients undergoing hemodialysis.

According to the results of ROC analysis, fibroblast growth factor-23 was found to be a more reliable prognostic factor compared to other laboratory indicators (AUC=0.65, $p<0.05$). These results confirm the appropriateness of using FGF-23 as a biomarker with relatively high clinical significance in assessing survival in patients undergoing hemodialysis.

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