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Factors Influencing The Favorability Of Patients With Renal Transfer

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Abstract. The article comparatively examines the factors affecting survival in patients who underwent kidney transplantation. The research results confirmed the dependence of survival and transplant loss after kidney transplantation on a number of factors. Among them, age, male sex, long-term dialysis, smoking, diabetes mellitus, chronic heart failure, arterial hypertension, and obesity significantly increase the risk. Insufficient immunosuppression, especially the low dose of tacrolimus, had a serious negative impact on the survival of the transplant. These data confirm that the early detection of high-risk patients, individual monitoring, and optimization of immunosuppressive therapy are crucial for increasing transplant survival. The obtained results confirm the need for a comprehensive approach to assessing post-transplant risk, taking into account clinical, immunological, and transplant-related factors, and not a single factor.
Keywords: chronic kidney disease, fibroblast-23, parathyroid hormone, vitamin D, viability.

Introduction. Kidney transplantation in chronic kidney disease (CKD) with progressive and irreversible changes remains a widely discussed area today. A glomerular filtration rate of less than 30 ml per minute per 1.73 m2 of body surface area is an indication for kidney transplantation [33].

In the last decade, the number of patients receiving kidney transplants has been steadily increasing, which, in turn, has led to the emergence of new and complex issues. This method is considered an alternative treatment for end-stage renal failure and is being increasingly implemented in all countries, including our Republic [1].

In 2018, successful kidney transplants were performed on 36,541 people in the United States of America, 27,917 in Europe, 18,505 in the Western Pacific region, 8,604 in Southeast Asia, 3,207 in Eastern Mediterranean countries, and 705 in Africa [2,3]. The extent to which patients adhere to doctors' recommendations has been reflected in several articles published abroad in recent years. These chronic patients must follow the recommended procedures and treatment measures to prevent the risk of transplant rejection, reduce the likelihood of exacerbation of concomitant diseases, and minimize the development of new complications. The recommended measures are comprehensive, including non-pharmacological treatments such as smoking cessation, avoiding alcohol abuse, regular physical activity, as well as the use of immunosuppressive drugs [4].

One study showed that 28% to 67% of patients (depending on the detection method) did not adhere to the immunosuppressant regimen [5,6]. As a result, the probability of transplant rejection in recipients increased sevenfold, along with pronounced acute rejection, increased morbidity, and high additional costs for the healthcare system [7,8].

In several medical centers in the capital of our republic and among the regions, the Samarkand Regional Medical Center is one of the first to successfully perform kidney transplant operations. It is known that this method is considered the most effective and promising approach for providing medical care to patients in the terminal stage of chronic kidney disease and undoubtedly has a number of advantages over hemodialysis and peritoneal dialysis. At the same time, there are psychological problems associated with certain limitations in

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the life of a kidney transplant patient. These include frequent doctor visits, strict adherence to the regimen of taking immunosuppressant drugs and concerns about their side effects, uncertainty about future life, the possibility of infection, and the risk of transplant rejection in case of crisis. Therefore, studying the quality of life of kidney transplant recipients and obtaining information about it creates an opportunity to conduct further therapeutic procedures and provide targeted counseling before transplantation [13,14,15].

In 2023, more than 300 patients underwent kidney transplantation in our country. Afterwards, the improvement in patients' quality of life and its duration compared to hemodialysis and peritoneal dialysis has been fully proven and is universally recognized by all specialists.

The survival of kidney transplant patients is influenced not only by external factors, but also by a number of internal factors, particularly some laboratory changes. Taking this into account, we studied the interaction of several laboratory parameters in patients with kidney transplants.

One of them is fibroblast growth factor 23 (FGF-23), a protein consisting of 251 amino acids weighing 32 kDa, which is synthesized and secreted by bone cells - mainly osteoblasts [16,17]. Unlike other proteins in this class, FGF-23 contains a signal peptide and has low affinity for heparin. It spreads throughout the body via the bloodstream and affects specific areas, including the kidneys.

Administration of 1,25- (OH) 2D increases circulating FGF-23 levels in the blood [19]. According to some data, an increase in blood FGF-23 begins at stage 2 CKD, before changes in calcium, phosphorus, and parathyroid hormone levels are observed [20]. In the terminal stage of CKD, its level in most cases increases from 100 to 1000 times the normal range [21]. A significant increase in FGF-23 in CKD is explained by an increase in its secretion and a decrease in its clearance from the bloodstream. This condition occurs with the development of pronounced hyperphosphatemia and vascular calcification, as well as severe renal failure, despite measures to prevent a significant increase in FGF-23 [22].

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 [23].

An increase in parathyroid hormone (PTH) in the blood parallel to a decrease in kidney function is often one of the early detectable changes [24]. Mortality from cardiovascular diseases is higher in patients with elevated PTH levels. According to statistical data provided by Hagström et al., in observations of 958 elderly people, it was noted that a 1-SD increase in serum PTH increased the risk of death from cardiovascular diseases by 37-38% [25].

Several mechanisms can explain the relationship between PTH and mortality from cardiovascular diseases. Primarily, PTH directly participates in the processes of atherogenesis through vascular calcification and remodeling [26,27]. This hormone also causes left ventricular myocardial hypertrophy, cardiac calcification, and fibrosis, negatively affecting the heart [28]. In addition, PTH may be involved in the pathophysiological mechanisms of hyperglycemia observed in CKD.

Along with the above, a reliable correlation was found in patients between moderate to high left ventricular myocardial mass and low ejection fraction with serum FGF-23 levels, independent of β-type natriuretic peptide and cardiac T-troponins [29].

It is known that currently, the non-specific inflammatory marker C-reactive protein is considered an appropriate biomarker of endothelial dysfunction in CKD [30]. Endothelial dysfunction, along with monocyte adhesion, reduced nitric oxide production, and decreased vasodilation activity, is associated with the development of early atherosclerosis [31].

Although some clinical observations suggest that FGF-23 is associated with increased C-reactive protein levels in CKD, there is insufficient data regarding its direct inducing effect on endothelial dysfunction [32].

Purpose of the study: Assessment of factors influencing survival in patients with kidney transplantation in the Samarkand region.

Research materials and methods: The study involved 90 patients who underwent kidney transplantation in the Samarkand region. Their average age was 52.6±4.60 years, and there were 58 men and 32 women. All patients were under full observation, and the procedure for receiving treatment was studied.

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The subjects underwent a general blood and urine analysis, biochemical studies (urea, creatinine, albumin, etc.), as well as vitamin D, parathyroid hormone, fibroblast-23.

Analysis of the research results. In the course of our study, a mutual logistic regression analysis of the factors influencing the acceptance of the transplant by the body in early stages or their viability in late stages was conducted in patients who underwent kidney transplantation, and the obtained results are presented in Table 1.

Table 1.

One-factor logistic regression analysis of factors influencing the survival of patients with kidney transplantation or transplant loss

Variables	OR (odds ratio)	95% CI (Confidence interval)	P (Reliability)
Age, years	1.46	1.32-1.67	< 0.001
Sex, male	1.22	1.08-1.42	0.012
Smoking tobacco	1.42	1.25-1.86	< 0.001
Duration of dialysis before transplantation, years	1.34	1.22-1.53	< 0.001
Diabetes	1.90	1.57-2.34	< 0.001
Chronic heart failure	2.23	1.80-2.84	< 0.001
Hypertension	1.24	1.12-1.45	0.006
Ischemic heart disease	1.75	1.40-2.15	< 0.001
Body mass index, over 30 kg/m2	1.40	1.20-1.75	0.003
Panel-reactive antibody compatibility greater than 50%	2.46	1.98-3.20	< 0.001
Low Tacrolamic dose	2.92	1.52-2.54	<0.001
Donor age	1.26	1.14-1.42	<0.001
Transplanted kidney (KDPI) status ≥85	2.12	1.73-2.82	<0.001

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DGF (transplanted kidney failure to function immediately after surgery)	2.76	2.23-4.10	<0.001
Sharp member rejection	3.12	2.48-4.0	<0.001
Cytomegalovirus infection	1.62	1.32-2.15	<0.001
VK virus nephropathy	3.55	2.64-4.72	<0.001

As can be seen from the table, the risk of death or loss of the transplant in patients with kidney transplantation increases significantly with age (OR = 1.46, 95% CI 1.32-1.67, p<0.001). The obtained results indicate that cardiovascular complications and immunological reactions are more common in older recipients. When comparing men with women, the observed risk of death was 22% higher (OR = 1.22, 95% CI 1.08-1.42, p<0.01). This is due to the higher incidence of cardiovascular diseases in men and the presence of harmful habits.

Conclusions close to our results have been proven in a number of studies. In particular, studies of Eurotransplant and US OPTN showed that the recipient's age and the duration of pre-transplant dialysis increase the risk of transplant dysfunction [34]. Long-term dialysis therapy leads to the development of vascular calcification, oxidative stress, and chronic systemic inflammation. This slows down the processes of transplant revascularization and increases the risk of renal dysfunction.

In smokers, these complications were found to be 42% higher (OR = 1.42, 95% CI 1.25-1.86, p<0.001). It was observed that prolonged dialysis before transplantation increases the incidence of calcification, anemia, and inflammation in the body (OR = 1.34, 95% CI 1.22-1.53, p<0.001), which has a highly significant negative effect on the transplant.

It was determined that the presence of diabetes mellitus in this group of patients poses a risk of almost 2 times (OR = 1.90, 95% CI 1.57-2.34, p<0.001) and chronic heart failure more than 2 times (OR = 2.23, 95% CI 1.80-2.84, p<0.001). It is known that the presence of diabetes mellitus weakens the immune system, increases infections and cardiovascular complications, and reduces the function of the transplanted organ. The presence of chronic heart failure leads to a deterioration of hemodynamics. Along with the above, it was noted that recipients with arterial hypertension have a 24% increased risk of developing sclerosis processes in the transplant arterioles (OR = 1.24, 95% CI 1.12-1.45, p<0.001). A body mass index above 30 kg/m2 increased the risk of developing infections and thrombosis, delayed wound healing, and negatively affected survival in 40% of cases (OR = 1.40, 95% CI 1.20-1.75, p<0.001).

Panel-reactive antibodies exceeding 50% in the recipient fight against the donor organ and lead to its rapid elimination from the body (OR = 2.46, 95% CI 1.98-3.20, p<0.001). Also, in our observations, it was found that the inadequate administration of immunosuppressive drugs, specifically tacrolimus, increases the risk by 3 times (OR = 2.92, 95% CI 1.52-2.54, p<0.001).

Among the factors dependent on the donor organism, their age (OR = 1.26, 95% CI 1.14-1.42, p<0.001) and the condition of the transplanted kidney (KDPI) played an important role (OR = 2.12, 95% CI 1.73-2.82, p<0.001).

Among the factors arising after kidney transplantation, DGF, i.e., delayed graft function, where the transplanted kidney does not start functioning immediately after surgery and the patient temporarily remains on hemodialysis, is one of the strongest negative factors (OR = 2.76; CI 2.23-4.10, p<0.001). This indicates acute ischemic damage to the nephrons and increases the risk of acute rejection by 2-4 times. Acute rejection was also noted to have a highly significant impact on graft failure (OR = 3.12; CI 2.48-4.0, p<0.001). It is known that cytomegalovirus infection reduces immunity in the recipient's body and intensifies the rejection

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process. The results we obtained also confirmed that this infection plays an important role in the transplantation process (OR = 1.62; CI 1.32-2.15, p<0.001).

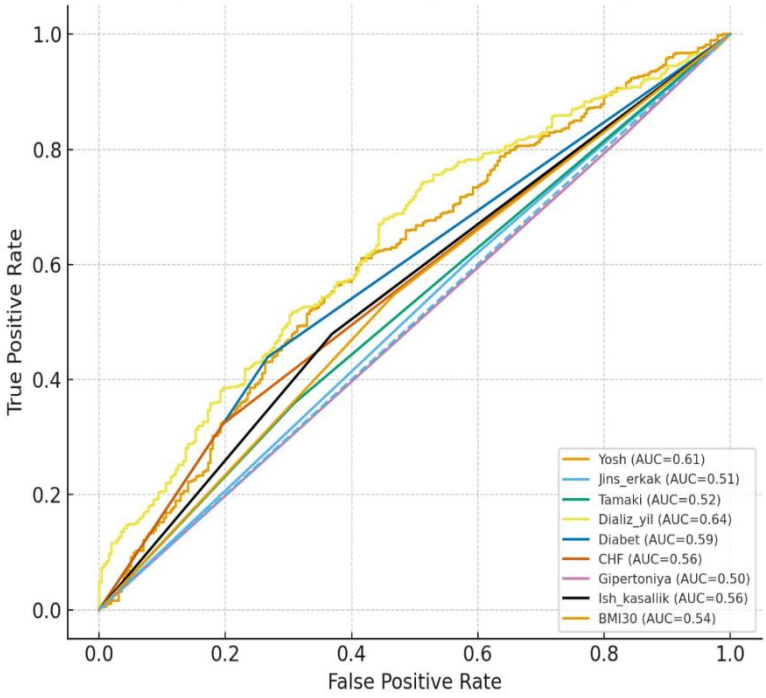
In addition, BK virus (human polyomavirus 1) nephropathy is also considered a high-risk factor, which increases the risk of transplant nephritis by 3.5 times (OR = 3.55; CI 2.64-4.72, p<0.001). According to recent data, BK virus-associated nephropathy leads to inevitable graft loss in 30-50% of cases [35]. Our results indicate an even higher relative risk (OR 3.55), which emphasizes the importance of preventing and early detection of immunosuppression.

Using the above results, we conducted a ROC analysis to determine the combined sensitivity and specificity of all the studied indicators in patients who underwent kidney transplantation, as well as their role in predicting survival, which is presented in Figure 1.

Figure 1. Joint ROC analysis of all factors influencing the survival of patients who underwent kidney transplantation.

As shown in the figure, based on the results of the multifactorial ROC analysis, it was noted that the studied indicators have a highly significant negative impact (AUC=0.822, p<0.001) on patient survival or rejection of the transplant.

At the next stage of our research, we assessed the impact of each identified indicator on survival in this group of patients using ROC analysis, and the obtained results are presented in Figure 2.



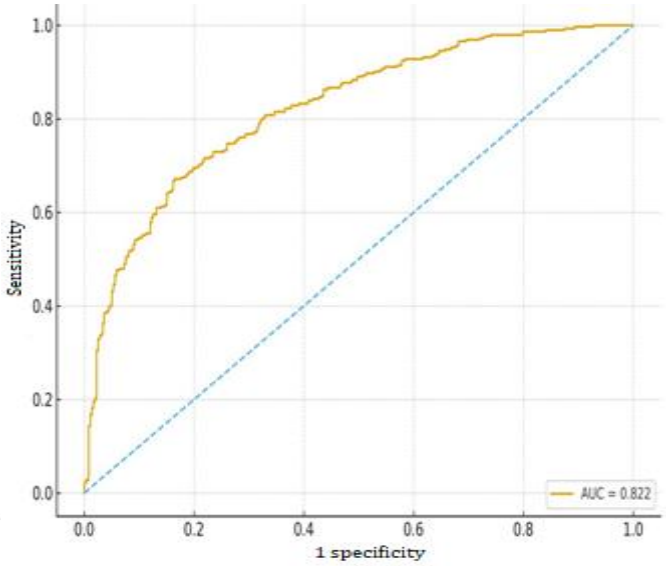


Fig. 2. ROC analysis of the main diseases affecting the survival of patients with kidney transplantation, as well as factors such as age and smoking.

This figure presents indicators of clinical and demographic factors in kidney transplant recipients, evaluated using ROC analysis for predicting post-transplant complications. AUC values ranged from 0.50 to 0.64, revealing that most factors have low to moderate predictive capacity. The dialysis period (AUC = 0.64) emerged as the strongest predictive factor in the analysis, with longer pre-transplant dialysis duration associated with more frequent complications. Patient age (AUC = 0.61) demonstrated moderate prognostic significance, aligning with the increased risk of complications in older recipients. Patients with diabetes mellitus (AUC = 0.59) face higher risks of infection, cardiovascular complications, and immediate post-operative graft failure. Chronic heart failure (AUC = 0.56) negatively impacts hemodynamic stability in patients. Although factors such as coronary heart disease (AUC = 0.56) and body mass index (AUC = 0.54) affect health, ROC analysis indicated their

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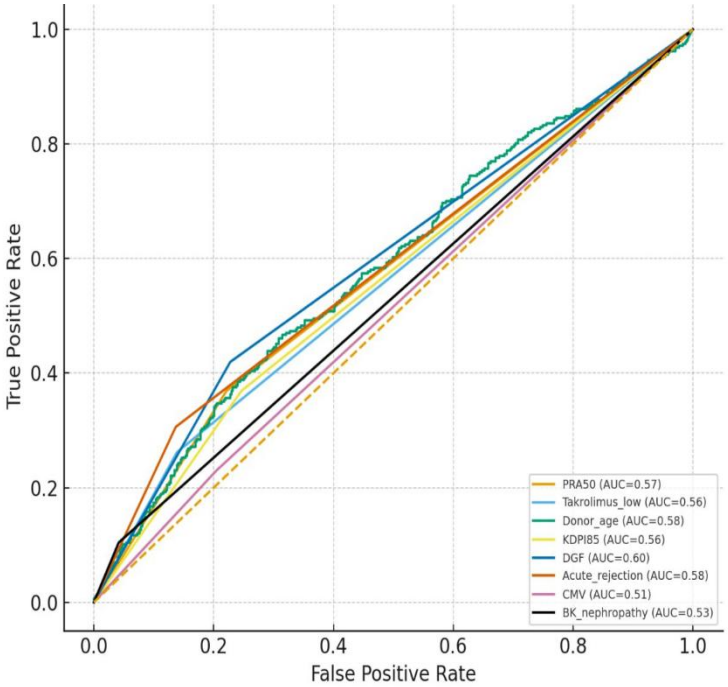
low predictive power. The clinical significance of factors including sex (AUC = 0.51), smoking (AUC = 0.52), and hypertension (AUC = 0.50) was found to be low.

Therefore, to accurately predict complications after kidney transplantation, it is advisable to use multifactorial forecasting models that combine several factors. Taking into account the above, we combined the factors studied in our study and conducted a ROC analysis of each biochemical factor, which is presented in Figure 3.

Fig. 3. ROC analysis of each biochemical factor influencing the survival of patients with kidney transplantation.



In this figure, the predictive value of immunological and donor-related factors after kidney transplantation is assessed based on ROC analysis. According to the analysis results, the AUC values of all studied markers fall within the range of 0.51-0.60, indicating their low clinical predictive ability when considered individually. This suggests that they are effective only when applied within a multivariate model.

In the analysis, the highest AUC value among all factors was observed for DGF (Delayed Graft Function), which occurs when the transplanted kidney does not function immediately after the operation (AUC = 0.60). This allows it to be used as a relatively reliable factor in predicting post-transplant complications. Additionally, panel-reactive antibodies above 50% (AUC = 0.57), low tacrolimus levels (AUC = 0.56), donor age (AUC = 0.58), transplanted kidney status (KDPI) ≥85 (AUC = 0.56), and acute rejection (AUC = 0.58) were evaluated as moderately strong predictors.

It was determined that CMV infection (AUC = 0.51) and BK virus nephropathy (AUC = 0.53) have low prognostic significance (AUC=0.5).

The results of the ROC analysis demonstrate that relying on single markers for predicting kidney transplantation outcomes does not allow for accurate conclusions. Our observations confirmed the advisability of using complex prediction models that incorporate multiple clinical, laboratory, and donor-related indicators.

Conclusion: The study results revealed that several factors influence patient survival after kidney transplantation. Among recipient-specific factors, age, male sex, long-term dialysis, smoking, diabetes mellitus, chronic heart failure, arterial hypertension, obesity, and high plasma renin activity significantly increase the risk. Insufficient immunosuppression, especially low tacrolimus doses, has a serious negative impact on graft survival. The donor's age and high KDPI score are also associated with graft dysfunction. Among post-transplantation factors, delayed graft function (DGF), acute rejection, CMV infection, and BK virus nephropathy were identified as the most potent adverse factors. These data confirm that early identification of high-risk patients, individualized monitoring, and adjustment of immunosuppressive therapy are of crucial importance in improving graft viability.

According to the ROC analysis results, the highest discriminatory ability in predicting post-transplant complications was observed for the DGF (Delayed Graft Function) factor (AUC = 0.60), allowing its use as a relatively more reliable prognostic indicator. Panel-reactive antibodies above 50%, donor age, acute rejection, low tacrolimus levels, and KDPI ≥85 were assessed as moderately predictive factors (AUC 0.56-0.58).

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Meanwhile, cytomegalovirus infection and BK virus nephropathy showed low discriminatory significance (AUC ≈0.5), indicating that they are insufficient as standalone reliable prognostic factors. These results confirm the need to apply a comprehensive approach to assessing post-transplant risk, considering not just a single factor, but a combination of clinical, immunological, and graft-related factors.

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