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### Research article

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### Malignancies in renal transplant recipients: A retrospective single-center descriptive study

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**Abstract.** *The risk of malignancy development in kidney transplant recipients (KTRs) is 2-3 times higher than in the general population. This picture, which emerged with chronic immunosuppressive use, has become more prominent in recent years as the ongoing cause of death in this population. This study aims to determine the common features of KTRs with malignancy in follow-up under a single-center experience. Thus, it is to save time by correctly determining our focus points in patient follow-up.*

**Methods.** *The files of 403 patients who underwent kidney transplantation between 2005 and 2020 in our hospital were reviewed retrospectively. The clinical findings at admission were age, gender, primary disease, use of cyclophosphamide before transplant, duration of dialysis, number of human leukocyte antigen mismatch, transplantation time, previous rejection, the existence of associated viral infections, comorbid diseases, used induction therapy, maintenance immunosuppressive therapy, allograft survival, recipient survival, malignancy development time after transplantation, serum creatinine, glomerular filtration rate (GFR) and presence of proteinuria and hematuria. Using these data, we retrospectively analyzed the incidence and types of malignancies in KTRs.*

**Results.** *During the follow-up period, 22 cancer cases have been developed. The median age of the patient was 60 years (IQR 45-64.3) and patients were mostly male (77.3%). The median follow-up period was 111.5 months (IQR 76.3-128.3). The median duration of dialysis was 54 months (IQR 11.5-78). The etiology of primary kidney disease in most KTRs recipients was unknown. The percentage of patients with mismatch 3 and above 3 was 86.3%. While the majority of patients received anti-thymocyte globulin (86.4%) as induction therapy, maintenance therapy was mostly tacrolimus + mycophenolate mofetil + prednisolone (86.4%). The median time from transplantation to the initial malignancy was 17.5 months (IQR 5-61.3). The most common initial malignancy was skin cancer (22.7%), followed by renal cell carcinoma originating from the native kidney (18.2%).*

**Conclusion.** *Renal transplantation is the most favorable renal replacement therapy. Malignancies are now among the important causes of death in KTRs and these patients have a higher risk of developing cancer than the general population. Therefore, screening for cancer at certain intervals, especially in long-term and elderly recipients after transplantation, will positively affect the survival of the patient and functional renal graft.*

**Key words:** renal transplantation, renal transplant recipients, malignancy, risk, mortality.

**Conflict of interest statement.** The authors declare no competing interest.

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## Злоякісні новоутворення у реципієнтів трансплантованої нирки: ретроспективне одноцентрове описове дослідження

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**Резюме.** Ризик розвитку злоякісного новоутворення у реципієнтів трансплантованої нирки (РТН) є у 2-3 рази вищим, ніж у загальній популяції, що обумовлено постійним застосуванням імуносупресивних засобів та є частою причиною смерті в цій популяції. Це дослідження має на меті визначити загальні клінічні риси РТН зі злоякісними новоутвореннями, що дозволить заощадити час, правильно визначаючи точки фокусування під час спостереження за пацієнтами.

**Методи.** Ретроспективно було проаналізовано медичну документацію 403 пацієнтів, яким була проведена трансплантація нирки в період з 2005 по 2020 роки. Точками інтересу були вік, стать, первинне захворювання, застосування циклофосфаміду перед трансплантацією, тривалість діалізу, кількість невідповідності антигену лейкоцитів людини, час трансплантації, попереднє відторгнення, наявність супутніх вірусних інфекцій, супутні захворювання, використана індукційна терапія, підтримуюча імуносупресивна терапія, виживання алотрансплантата, виживання реципієнта, час розвитку злоякісного новоутворення після трансплантації, сироватковий креатинін, швидкість клубочкової фільтрації (ШКФ) і наявність протеїнурії та гематурії. Використовуючи ці дані, ми ретроспективно проаналізували частоту та типи злоякісних новоутворень у КТР.

**Результати.** За період спостереження було виявлено 22 випадки злоякісного новоутворення. Середній вік пацієнтів становив 60 років (IQR 45-64,3), пацієнти переважно були чоловіками (77,3%). Середній період спостереження становив 111,5 місяців (IQR 76,3-128,3). Середня тривалість діалізу склала 54 місяці (IQR 11,5-78). Етіологія первинного захворювання нирок у більшості реципієнтів КТР була невідома. У той час як більшість пацієнтів отримували антитимоцитарний глобулін (86,4 %) як індукційну терапію, підтримуюча терапія була переважно такролімус + мікофенолат мофетил + преднізолон (86,4 %). Середній час від трансплантації до утворення злоякісної пухлини становив 17,5 місяців (IQR 5-61,3). Найпоширенішими злоякісними новоутвореннями були рак шкіри (22,7%) та нирково-клітинна карцинома, що походить від нативної нирки (18,2%).

**Висновок.** Злоякісні новоутворення на сьогодні є однією з важливих причин смерті у РТН. Онкологічний скринінг через певні проміжки часу, особливо у довгострокових реципієнтів та реципієнтів літнього віку позитивно вплине на виживання пацієнта та функціонування ниркового трансплантата.

**Ключові слова:** трансплантація нирки, реципієнт, злоякісні новоутворення, ризик, смертність.

**Introduction.** Kidney transplantation is a modality of kidney replacement therapy with the longest survival and the best quality of life in patients with end-stage renal disease (ESRD). Worldwide, the number of organ transplantation has increased from 19,864 in the year 2000 to 102,664 in 2017, and kidney and liver transplantation account for about 90% of total transplantations [1, 2]. As a result, an increased risk of a wide variety of cancers associated with solid organ transplantation has been observed. The most comprehensive data comes from a cohort study that analyzed the prevalence of malignancy in more than 175,000 solid organ transplant recipients between 1987 and 2008. The most common organs transplanted in-

cluded the kidney, liver, heart, and lung (in 58, 22, 10, and 4 percent of cases, respectively) [3]. With the advancement of transplantation surgical techniques and the development of potent immunosuppressive agents such as calcineurin inhibitors (CNIs) for maintenance therapy after transplantation, the life expectancy of patients was prolonged and the percentage of long-term functioning kidney grafts increased. However, kidney transplant recipients have suffered from significant complications, particularly cardiovascular disease and cancer [4].

The cumulative incidence of solid organ cancers after kidney transplantation increases 4-5% after the first 5 years, 10% after 10 years, and more than 25% after 20 years [5, 6, 7]. Compared with the general population the European Renal Association-European Dialysis and Transplantation Association (ERA-EDTA) registry showed that the standardized mortality ratio (SMR) for cancer was 1.7 (95% CI 1.6-1.8) among 44,540 transplant recipients. In addition, in the ERA-EDTA cohort, transplant recipients aged 20-29 years had the lowest rate of cancer mortality at 0.5 deaths per

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1,000 patient-years, which increased progressively to 25.6 deaths per 1,000 patient-years in recipients aged >80 [8].

Analysis of all cancers found that the average age at diagnosis was 40 years and the average delay was approximately three to five years after transplantation [9-11]. Kaposi sarcoma is 300-fold among kidney transplant recipients, non-melanoma skin cancers 2-40 fold, lip cancer 10 fold compared to the general population. It has been reported that cancers with viral oncogenesis as a proposed pathogenic mechanism such as post-transplant lymphoproliferative disorder (PTLD) are 4-16 times more common [3, 5, 6, 12-14]. Incidence, mortality and risk factors for posttransplant malignancy (PTM), show significant ethnic and geographical differences. Non-melanoma skin cancer (NMSC) and non-Hodgkin lymphoma (NHL) are the most common PTMs in the United States and Europe [3, 6, 13, 15]. In contrast, stomach and kidney cancers are commonly reported PTMs in Asian countries [16-18]. In a retrospective cohort study by Jeong S et al. comprehensive information on PTMs in East Asia was provided using a national population-based database. A total of 9915 kidney recipients between 2003 and 2016 were included. During this period, 598 cases (6.0%) of de novo PTMs occurred. The most common PTM was thyroid cancer (14.2%), followed by colorectal (11.2%), kidney (10.7%), and stomach cancers (8.9%). The standardized incidence ratio for all-site cancer was 3.9. The risks of Kaposi sarcoma and kidney cancer were more than 10 times those of the general population (13.5%), NHL (12.4%), stomach cancer (9.0%), and colorectal cancer (7.9%). In this study, while advanced age and graft dysfunction were correlated with the risk of development of PTM the geographical difference in the frequency percentage of the cancer type was also noted [19]. In a nested case-control study of 12,805 KTRs, Van de Wetering et al reported that 56% of all deaths in patients with a functioning renal graft were due to malignancy [20].

The reasons for the higher rate of cancer mortality in kidney transplantation compared to the general population may be due to differences in tumor biology due to immunosuppression, accompanying comorbid diseases, and the time of clinical onset [7, 21]. Secondary malignancies that develop in transplant recipients have been attributed to several factors including sun exposure, concurrent viral infection, pre-transplant dialysis, notably the extent and duration of immunosuppressive therapy. At least four viruses may be cocarcinogenic in transplanted patients, including Epstein-Barr virus (EBV), human herpesvirus 8 (HHV-8), human papillomavirus (HPV), and the Merkel cell polyomavirus (MCV). In rare cases, malignancy has been transplanted from the donor but can cause metastatic cancer in the immunocompromised transplant recipient. The risk of inadvertently transplanting malignant cells appears to depend on the type and extent of the donor's cancer [22].

Consequently, it has not been clearly proven that a particular immunosuppressive regimen increases or decreases risk. In fact, cancer risk is more related to the dose and duration of the medication regimen. In addition to the immunosuppressive drugs used, other risk factors we should pay attention to such as age, history of smoking, underlying kidney disease and history of prior cancers [15, 23, 24, 25]. De novo malignancies in transplant recipients have an aggressive course and higher mortality rate compared to the general population. Although treatment and follow-up strategies are largely based on general population data, the more accurate approach is to personalize each recipient according to current risk factors [26]. Therefore, periodic cancer screening and prophylactic measures are essential in the transplant patient to prevent and detect malignancies. The American Transplantation Association Clinical Practice Guidelines Committee has published recommended guidelines for cancer screening in kidney transplant patients [27]. The approach to PTM begins with general preventive measures. First, excessive immunosuppression or repeated exposure to antilymphocyte drugs should be avoided and careful screening of the patient and donor should be done prior to transplantation to help detect malignancy.

If malignancy is detected, immunosuppressive therapy may need to be reduced, changed, or even discontinued. Here the priority is the life of the patient, the graft can be sacrificed. For patients with pre-existing tumors, the recommendations that determine the probability of recurrence according to the tumor type are followed and alternative treatment approaches are determined with the approval of the oncologist. This group of patients should be followed more closely. However, any changes in immunosuppressive regimens should be prepared for the risk of allograft rejection or impaired renal function. Although there are rules accepted in the general population, the risk of cancer in this group of patients should always be evaluated with a personalized approach, taking into account the concurrent comorbidities [13, 15, 23-25].

**Subjects and Methods.** The files of 403 patients who underwent kidney transplantation between 2005 and 2020 in our hospital were reviewed retrospectively. After exclusion of the patients with graft removal (n=4) and who died (n=9) in this period, the study population was comprised of 390 KTRs. The following data at admission and follow-up including clinical and laboratory findings were obtained from medical records. The clinical findings at admission were age, gender, primary disease, use of cyclophosphamide before transplant, duration of dialysis, number of human leukocyte antigen mismatch, transplantation time, previous rejection, the existence of associated viral infections, comorbid diseases, maintenance of immunosuppressive therapy, used induction therapy, allograft survival, recipient survival, malignancy development time after transplantation, serum creatinine, GFR, presence of proteinuria and hematuria. Using these data, we retrospectively

analyzed the incidence and types of malignancies in KTRs. Induction therapy consisted of basiliximab (chimeric monoclonal antibody against interleukin 2), anti-thymocyte globulin (ATG) and methylprednisolone based on individual immunologic risk. Maintenance treatment comprised CNIs (cyclosporine A (CYC) or tacrolimus (TAC) or inhibitors of mammalian target of sirolimus (sirolimus or everolimus), mycophenolate mofetil (MMF), and prednisolone (DC). If the patient has a past history of BK virus, Epstein-Barr virus, cytomegalovirus, parvovirus, hepatitis B and hepatitis C infection, they are included in the relevant viral infection group. Over 2 erythrocytes in the urine were accepted as hematuria and 1 (+) above as proteinuria.

However, although not all tests have been performed for each patient due to personal conditions, the general approach was monitoring patients by performing a clinical examination, esophagogastroduodenoscopy, abdominal ultrasonography and fecal occult blood test at least once a year. For female patients, we recommended Papanicolaou smear test, mammography and breast ultrasonography yearly and tumor markers and computed tomography (CT) yearly for patients over 50-years-old. All patients with chronic hepatitis B or C received antiviral therapy and achieved sustained acceptable viral response before renal transplantation. AFP and liver sonography are checked every 3 months for this group. In the follow-up period, observation of microscopic or gross hematuria is verified with cystoscopy. Testing for serum PSA level for male KTRs are arranged. Patients with pretransplant native kidney cysts were checked by annual ultrasonography after renal transplantation.

Continuous variables are expressed as medians and interquartile ranges (IQRs). Categorical variables are summarized as frequency and percentage.

**Results.** During the follow-up period, 22 cancer cases have been developed (Table 1).

As presented in Table 1, the median age of patients was 60 years (IQR 45-64.3) and patients were mostly male (77.3%). The median follow-up period was 111.5 months (IQR 76.3-128.3). The median duration of dialysis was 54 months (IQR 11.5-78). The etiology of primary kidney disease in most KTRs was unknown. A total of 15 KTRs (68.2%) underwent renal replacement therapy from living donors. Panel reactive antibody (PRA) was over 30% in 4 patients before transplantation. Cyclophosphamide was administered to a single patient prior to the transplant. One patient had been operated on with the diagnosis of renal cell carcinoma (RCC) 5 years before the transplant. The percentage of patients with mismatch 3 and above 3 was 86.3%. Only 4 patients had a history of viral infection. The acute rejection period was present in 18.2%. While the majority of patients received ATG (86.4%) as induction therapy, maintenance therapy was mostly TAC + MMF + DC regimen (86.4%). The median serum creatinine of patients was 1.44 (IQR 1.1-2.3) and median eGFR was 48.5 (IQR 31.5-69.3). The percentage of co-morbid

diseases in patients was 13.6% for diabetes, 77.3% for hypertension and 22.7% for coronary heart disease, respectively. In the follow-up, 59.1% of the patients had proteinuria and none of them had hematuria.

The median time from transplantation to the initial malignancy was 17.5 months (IQR 5-61.3).

RCC was detected in native kidneys in 4 patients. Basal cell carcinoma (BCC) was detected in 2 patients and squamous cell carcinoma (SCC) was detected in 1 patient, while both BCC and SCC were detected in 2 patients at consecutive times. Two patients diagnosed with lymphoma did not have a history of viral infection. Laryngeal cancer was detected in one patient and medulloblastoma in another patient. Both patients with prostate cancer were over 75 years old. One patient had endometrial cancer, 2 had thyroid papillary cancer, 2 had gastric cancer and 2 had lung cancer. A total of four patients died after the diagnosis of cancer. Among these patients, the patient diagnosed with BCC died of pancreatitis 30 months later. Another patient committed suicide about a month after being diagnosed with lymphoma. Another patient who had nephrectomy with the diagnosis of RCC 5 years ago and received oncology approval before transplantation died 10 months after transplantation, probably due to lung metastasis of RCC. The last patient diagnosed with gastric cancer eight years after kidney transplantation, died of multiple organ failure due to diffuse metastasis 3 months after diagnosis.

**Discussion.** Malignancies are the second most common cause of mortality and morbidity in recipients after kidney transplantation. Also, kidney transplant recipients are twice as likely to develop cancer and die as the general population. Therefore, both donors and recipients should be screened for possible malignancy during the transplant preparation process. Potential recipients with previous cancer history should wait 2-5 years before transplantation, depending on the type and course of cancer [4]. Despite the remarkable burden of cancer, donors or recipients do not have a detailed screening and guide for cancer. Unfortunately, treatment protocols applied to the general population are valid for cancers detected after transplantation. When modifying the immunosuppressive regimen in PTM, the risk of allograft rejection or deterioration should also be taken into account and the treatment should be arranged to maintain the balance of both conditions [28].

Interestingly, a large cohort study showed that a history of previous malignancy does not have an additive effect on cancer-specific and all-cause mortality in KTRs who develop cancer [29]. A recent study reported that RCC is associated with a variety of etiologies, including demographic features, dialysis duration, medical indications for transplantation and kidney failure function [30]. Studies have determined that age and gender are risk factors for cancer in transplant recipients. Among recipients at the transplant age 55, the 5-year absolute cancer risk is at least three times higher than the group <35 years of age [31].

Table 1

## The patients' demographic and clinic characteristics:

	Sex	Age	Etiology	HD time (months)	Tx time (months)	Donor	Mismatch	Induction therapy	Maintenance therapy	GFR	Malignancy time	Cancer type	Survival
Patient 1	M	68	PKB	3	96	LD	6	ATG	TAC+MMF+DC	19	60	BCC	EX
Patient 2	M	64	Unknown	72	61	CD	5	ATG	TAC+MMF+DC	19	26	SCC	AL
Patient 3	M	65	Unknown	60	79	CD	6	ATG	TAC+MMF+DC	36	19	BCC	AL
Patient 4	M	62	HT	7	86	LD	5	ATG	TAC+MMF+DC	30	16	SCC	AL
Patient 5	M	37	I.N	6	123	LD	3	ATG	TAC+MMF+DC	32	20	Lymphoma	EX
Patient 6	M	38	Unknown	36	120	LD	4	ATG	CYC+MMF+DC	19	60	Medulloblastoma	AL
Patient 7	F	62	Unknown	3	108	LD	6	ATG	TAC+MMF+DC	44	3	Laryngeal cancer	AL
Patient 8	M	76	Unknown	60	152	LD	3	ATG	TAC+MMF+DC	52	120	Prostat Ca	AL
Patient 9	M	48	Unknown	28	117	CD	2	ATG	TAC+MMF+DC	9	3	Small Cell ca	AL
Patient 10	M	46	Unknown	60	162	LD	3	ATG	mTOR +MMF+DC	74	108	RCC(nativ)	AL
Patient 11	M	45	Soliter Kidney	30	10	LD	3	Basiliximab	TAC+MMF+DC	93	10	Small Cell ca	EX
Patient 12	M	77	Unknown	144	144	CD	3	ATG	TAC+MMF+DC	69	15	Prostat Ca	AL
Patient 13	M	45	Unknown	preemptive	68	LD	4	ATG	TAC+MMF+DC	87	49	Endometr um Ca	AL
Patient 14	F	65	Unknown	129	40	LD	6	ATG	TAC+MMF+DC	45	6	Thyriod Papiller Ca	AL
Patient 15	F	58	Piyelonephritis	60	132	LD	5	ATG	TAC+MMF+DC	65	36	RCC(nativ)	AL
Patient 16	M	49	cGN	144	125	LD	3	Basiliximab	TAC+MMF+DC	43	10	RCC(nativ)	AL
Patient 17	M	29	Unknown	13	132	LD	3	Basiliximab	TAC+MMF+DC	70	5	Thyriod Papiller Ca	AL
Patient 18	F	34	Unknown	60	54	CD	2	ATG	TAC+MMF+DC	58	5	RCC(nativ)	AL
Patient 19	M	59	Unknown	106	115	CD	4	ATG	TAC+MMF+DC	59	5	BCC	AL
Patient 20	M	61	Unknown	48	96	CD	0	ATG	TAC+MMF+DC	38	3	GASTRIC CANCER	EX
Patient 21	F	62	PKD	96	91	LD	6	ATG	CYC+MMF+DC	58	65	Lymphoma	AL
Patient 22	M	62	Unknown	42	127	LD	4	ATG	TAC+MMF+DC	77	84	GASTRIC CANCER	AL

Abbreviation: M, male; F, female; PKD, polycystic kidney disease; IN, interstitial nephritis; HD, hemodialysis; GN, crescentic glomerulonephritis; HT, hypertension; LD, living donor; CD, cadaveric donor; ATG, anti-thymocyte globulin; DC, dactacortil; MMF, mycophenolate mofetil; TAC, tacrolimus; CYC, cyclosporin; GFR, glomerular filtration rate; BCC, basal cell carcinoma; SCC, squam z cell carcinoma; RCC, renal cell carcinoma; EX, exitus; AL, alive.

However, there is a higher relative risk of cancer in younger transplant recipients due to low cancer incidence at a young age in the general population. Therefore, compared to the general population, the relative risk of cancer in young transplant recipients under 30 years of age was 10 times higher, whereas in recipients over 55 years of age this risk was only two to three times higher [25, 31, 32]. In addition, male transplant recipients have a 20-30% higher cancer risk than women overall [24, 33]. Similarly, in our study, the median age of the patient was 60 years and patients were mostly male (77.3%).

There is a dose-dependent relationship between CNIs and secondary malignancies. Limited evidence from animal experiments suggests that CYC can promote cancer progression through the production of transforming growth factor-beta (TGF-beta). In vitro, CYC induces invasive behavior of non-transformed cells with dramatic morphological changes; Additionally, administration of CYC supports tumor growth in immunodeficient animals [34, 35]. Data from one series suggest that the use of TAC increases the risk of malignancy following kidney transplantation [36]. TAC, like CYC appears to increase TGF-beta levels, which is clearly associated with tumor growth [37]. In addition, in prospective comparisons of CYC and TAC in kidney or liver transplantation, there was no difference between the two districts in cancer development after 3 or 5 years of follow-up. A direct cause-and-effect relationship between CNIs and cancer development is still a matter of debate [38, 39]. Also, the use of azathioprine has been associated with the development of neoplastic post-transplantation, particularly with an increased risk of cutaneous cancers [22]. Compared with other immunosuppressive medications, sirolimus has direct antitumor effects and reduces the risk of malignancy [40, 41, 42, 43, 44]. Several retrospective studies and case reports have described a variety of clinical outcomes following the transformation of mTOR inhibitor-based immunosuppression following a cancer diagnosis [45, 46]. In a study involving 15 kidney recipients, it was observed that the lesions regressed by replacing CYC with sirolimus after cancer diagnosis [47].

In another cohort study of 20 KTRs with post-transplant cancer, CNIs, azathioprine, or MMF were discontinued after sirolimus initiation and after a mean follow-up of 14 months, complete regression was observed in 4 patients with Kaposi's sarcoma and 2 patients with PTLN. On the other hand, it was found that the disease progressed in patients with advanced or extensive cancer. Allograft function was preserved in all patients except one with T-cell lymphoma [45]. The best data were derived from a systematic review and meta-analysis of randomized trials comparing immunosuppressive regimens with and without sirolimus in kidney and kidney-pancreas transplant recipients. Compared to controls, sirolimus provided a 40 percent reduction in overall risk and a 56 percent reduction in non-melanoma skin cancer risk. In contrast, analysis

of de novo sirolimus trials revealed no difference in malignancy risk between sirolimus and controls; however, sirolimus was associated with an increased risk of cardiovascular and infection-related mortality in this meta-analysis [48]. MMF impairs lymphocyte function by blocking purine biosynthesis through inhibition of inosine monophosphate dehydrogenase. Thus, by inhibiting this enzyme, which increases dramatically in some malignancies, it may create some antiproliferative effect and may actually be associated with a decreased risk [22, 49-51]. In two large registry studies [Organ Procurement and Transplantation Network/United Network for Organ Sharing (OPTN/UNOS) and Collaborative Transplant Study CTS], differences in cancer rates could not be demonstrated in mycophenolate-containing regimens when compared with mycophenolate-free regimens. In the MMF group, there was a trend toward a lower risk of malignancy in both registries [50]. However, complete cessation of CNIs therapy in patients who develop post-transplant cancer may affect both patient and graft survival. There are also studies showing that it will have a harmful effect. A multicenter, retrospective cohort study of 104 KTRs with PTLN demonstrated that discontinuation of CNI therapy was the most important risk factor for graft loss and patient death [52, 53]. Antibody therapy against T lymphocytes (such as OKT3 or antilymphocyte serum) predisposes to PTLN, particularly caused by EBV [30]. While the majority of patients received ATG (86,4 %) as induction therapy, our recipients' maintenance therapy was mostly TAC + MMF + DC regimen (86.4 %). Once PTM was detected, CNI treatment was converted to mTOR therapy in all of them.

Recipients with at least two donor-recipient HLA-DR mismatches have 24% higher rates of an increased risk of large B cell lymphoma (DLBCL) than those with nonHLA-DR mismatches. Certain recipient HLA alleles have been associated with altered post-transplant cancer risk [54]. The percentage of patients with mismatch 3 and above 3 was 86,3% and the acute rejection period was present in 18.2 % in our study.

Also, the long period of time the recipient spends on dialysis has been reported to increase the risk of possible cancer after transplantation [4, 31, 55]. In our study, the median duration of dialysis was 54 months.

It has been reported that cancer development is 50% higher in recipients transplanted from cadavers compared to recipients transplanted from living donors, especially kidney, urinary tract and gynecological cancers [56]. In our study, mostly cancer was observed in recipients transplanted from a living donor (68.2%). The reason for this may be more frequent kidney transplants from living donors in Turkey.

Cancer prevalence increases over time after kidney transplantation and compared to the same age and gender, the cancer frequency in this group is at least twice as high. Unfortunately, as there are no comprehensive guidelines for this particular patient group, treatment and follow-up guidelines are followed according to the

general population. Because cancer is a cause of substantial morbidity and mortality in kidney transplant recipients, the guidelines should be personalized for each patient in this population. Evaluation and management of cancer that develops after kidney transplantation is a complicated process that requires attention and care. The most important detail is that the dose of maintenance treatment is arranged in a way that prevents rejection and does not aggravate cancer. In addition, interactions of chemotherapeutics with immunosuppressive therapy, possible side effects, the physical and psychosocial adaptation of the recipient to the process should also be taken into account. The most important thing is the patient's survival during this period. The healthy functioning of the graft should be of secondary importance.

**Conclusions.** Studies on recipients who develop cancer after kidney transplantation shed light on patients within this group who deserve more careful

screening. In our study, we concluded that patients who have been on dialysis for a long time, who have more than 3 incompatibilities, who take ATG as induction therapy and who receive CNI for maintenance therapy should be screened more frequently for cancer. Thus, with a standard and personalized approach to screenings in identified risk groups. We anticipate that cancers detected in the early period will be treated in a shorter and more effective time, patient and graft survival will increase in the long term, and the patient's financial burden will be reduced.

**Conflict of interest statement.** The authors declare no competing interest.

**Authors Contributions.**

**Meral Meşe:** Writing the manuscript, data collection and clinical data analysis;

**Ergün Parmaksiz:** Writing the manuscript, data collection and research management.

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