Incidence and Risk Factors of Post-renal Transplantation Malignancies in North of Iran, A 20-year Experience

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Introduction. The main causes of death in kidney transplant recipients are cardiovascular diseases and malignancy. This study aimed to determine the types of post-transplant malignancy, incidence, and related factors in renal transplant recipients referred to Razi Hospital in Rasht, Iran.

Methods. This retrospective cross-sectional study was conducted on 549 kidney transplant recipients between 1998 and 2018. Patient-, transplant-, and medication-related factors and pathology reports were recorded in the check list. Chi-square, T-test and Logistic Regression were used to investigate the effect of variables. Malignancy-person-year incidence rate was calculated using survival tables and Kaplan-Mayer analysis.

Results. 43 (7.8%) recipients had malignancies. The most common site of malignancy was the skin (53.5%). Non-Melanoma Skin Cancer (NMSC) was the most common cancer (32.6%) followed by Kaposi sarcoma (20.9%). The standardized incidence ratio (SIR) of post-transplant malignancies in renal transplant recipients was 26.9 times the malignancies in Guilan province and 21.7 times the malignancies in Iran. Cox proportional hazard models identified older age at the time of transplantation and history of azathioprine consumption seems to be associated with risk for post-transplant malignancy.

Conclusion. The most common malignancies in these people were non-melanoma skin cancer, Kaposi sarcoma and then GI malignancies. According to the information obtained in this study, regular periodic examinations of kidney transplant recipients for early detection of malignancy is important.

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INTRODUCTION

Renal transplantation (RT) is generally accepted as the best treatment for patients with end-stage renal disease (ESRD) because it improves survival and quality of life.[1-3] After cardiovascular disease, malignancy is the second most common cause of mortality and morbidity in kidney transplant recipients (KTR).[2,4] They have at least twice higher risk of developing or dying from cancer than the age and gender match general population.[2,5] The cumulative incidence of solid organ cancers after RT increases from 4 to 5% after 5 years to 10% after 10 years and to > 25% after 20 years.[2]

The increased risk of de novo and recurrent cancer in transplant recipients is multifactorial and attributed to oncogenic viruses, immunosuppression

and altered T cell immunity.[2] Increased age at transplantation, male gender, white ethnicity, extended time on dialysis before transplantation, underlying cause of ESRD, sun exposure, prior history of malignancy, smoking, and alcohol consumption are key risk factors for the development of malignancy after transplantation.[2,6]

The increased risk of tumors after kidney transplantation does not include all malignancies such as breast, cervix, brain, and prostate cancer while it seems in melanoma and non-melanoma skin cancers, Kaposi sarcoma, lymphoma, colon, liver and lung cancer.[4] The growing burden of cancer is prompting physicians and policymakers to consider prevention, screening and treatment strategies in this high-risk population.[2] But regard to lack of randomized controlled trial studies, the treatment of these patients is associated with challenge.[5]

In this study, we investigate the incidence of various malignancies and related factors in kidney transplant recipients at Razi Hospital in Rasht over a period of twenty years.

MATERIALS AND METHODS

This retrospective cross-sectional study was conducted with census method on KTR who transplanted since 1998 to 2018 in the Razi hospital (Renal transplant center of Guilan, Northern Iran). The KTR which were transplanted at other centers but were followed up in this center, were also considered. The clinical study was reviewed and approved by the ethics committee of the Guilan University of Medical Sciences, Iran (No. IR.GUMS.REC.1397.234) and was performed in accordance with the Declaration of Helsinki. Informed consent was obtained from patients. The recipients who had malignancy before transplantation or ESRD due to malignancy, developed malignancy in less than one month after transplantation and patients with HIV were excluded from our study.

The recipients' demographic information was obtained from medical records. Those who did not seek follow-up after transplantation were contacted and asked about the history of malignancy. Patients with one type of post-renal transplantation malignancy were identified.

In case of malignancy, the date of diagnosis and the type of malignancy were recorded according to the pathologist's report.

Data was collected by the check Lists and demographics questionnaire. The characteristics and clinical data that recorded for all patients were patient's status (being alive or deceased), gender, age, age at transplantation, smoking, smoking cessation history(Less than five years/ Five years or more), family history of malignancy, Sun exposure (low, moderate, high), Duration of follow-up, Retransplantation, history of Malignancy, Anti-thymocyte globulin (ATG) and Daclizumab (Zenapax) (for induction) and maintenance immunosuppressive therapy as combination of drugs and effect of each drug separately.

At interview, subjects were asked how many hours they would normally have spent outdoors and at their jobs. Sun exposure was divided into three levels: low (Office work or contact < 2 hours a day), moderate (Jobs requiring traffic and open spaces or contact between 2 and 4 hours a day) and high (Working and agricultural occupations or contact > 4 hours a day in the open spaces).[7,8]

Data were analyzed using the computer software program Stata version 12 (Statacorp, TX, USA). Qualitative variables were expressed as number and percentage, while quantitative variables were shown by mean ± standard deviation (SD). Quantitative and qualitative variables were compared by Student *t*-test and chi-square and Fisher exact test as univariate analyses. Multivariate logistic regression backward model was used for incidence of malignancy. To measure the relative risk of cancer in transplant recipients compared to the general population, we calculated a standardized incidence ratio (SIR) (i.e., observed/ expected cases). 95% CIs for the SIR were achieved using a precise methods that assumes the observed counts follow a Poisson distribution. The Kaplan–Meier method was used to estimate the cumulative probability of malignancy development in the four age groups of patients (< 40 years; 41 to 50 years; 51 to 60 years, and > 60 years) during follow-up. Differences in survival time were calculated using the log rank test. Factors related to the occurrence of malignancy were assessed by univariate and multivariate analyses using Cox proportional hazard model. The P value < .05 was considered as a level of statistical significance and 95% CI was also considered to be a reliable estimate. We used a P value < .2 to enter variables into the multivariate regression model.

RESULTS

In total, 549 patients were included in the study. Of these, 7.8% had malignancy. The mean recipient age and recipient age at transplantation were 50.54 ± 14.20 and 40.91 ± 13.84 years. The majority of recipients were female (56.5%) and 92.3% were nonsmoker, 65.8% were self-employed, 63.8% had moderate sun exposure. Also, 85.8% of transplant patients survived. The mean duration of follow-up was 8.43 ± 5.25 years, so that the minimum survival time after transplantation was 6 months and the maximum survival period was 20 years. 96.2% of patients were transplanted only once and only 15% had a history of rejection. About 42.8% of patients had a history of ATG use as induction or antirejection therapy and 23.9% history of Zenapax taking as induction therapy. Also, the effects of maintenance drugs in combination are demonstrated in Table 1 and each drug separately in Table 2. The overall incidence of post-transplant malignancy (PTM) in our population was 7.8%. Skin malignancies were the most common cancers (53.5%). Among them, Non-Melanoma Skin Cancer (NMSC) (32.6%), and Kaposi sarcoma (20.9%) were most common form of skin cancer (Table 3).

Using Logistic Regression, the intervention agents entered the equation with the backward method and it was found that patient's age at the time of kidney transplantation and using azathioprine are the only variables that have intervening and

Table 1. Demographic and Clinical Characteristics of Kidney Transplant Recipients

Characteristics	Total Patients (n = 549)	Without Malignancy (n = 506)	With Malignancy (n = 43)	*P*
Gender of Recipient (Male/Female), %	(43.5 / 56.5)	(43.5 / 56.5)	(44.2 / 55.8)	> .05*
Recipient Age, y	50.54 ± 14.20	49.82 ± 14.04	59.72 ± 13.13	< .001†
Recipient Age at Transplant, y	40.91 ± 13.84	40.41 ± 13.76	47.19 ± 13.42	< .05†
Smoking (Yes/No), %	(7.7 / 92.3)	(7.5 / 92.5)	(9.3 / 90.7)	> .05*
Family History of Malignancy (Yes/No), %	(14.9 / 85.1)	(15.2 / 84.8)	(11.6 / 88.4)	> .05*
Job, %				
Farmer	10.7	10.1	18.6	> .05*
Self-employed	65.8	66.6	55.8	
Housewife	16.8	16.6	18.6	
Employee	6.7	6.7	7.0	
Sun Exposure %				
Low	20	20.6	14.0	> .05*
Moderate	63.8	63.2	69.8	
High	16.2	16.2	16.3	
Patient Status (Alive/Deceased), %	(85.8 / 14.2)	(88.5 / 11.5)	(53.5 / 46.5)	< .001*
Duration of Follow-up, y	8.43 ± 5.25	8.33 ± 5.18	9.62 ± 5.97	> .05†
Re-transplantation (Primary/Re-transplant), %	(96.2 / 3.8)	(96.0 / 4.0)	(97.7 / 2.3)	> .05*
Transplant Rejection (No/Yes), %	(84.7 / 15.3)	(84.4 / 15.6)	(88.4 / 11.6)	> .05*
ATG (Yes/No), %	(42.8 / 57.2)	(43.7 / 56.3)	(32.6 / 67.4)	> .05*
Zenapax (Yes/No), %	(23.9 / 76.1)	(23.3 / 76.7)	(30.2 / 69.8)	> .05*
D_1 (Yes/No), %	(63.9 / 36.1)	(63.6 / 36.4)	(67.4 / 32.6)	> .05*
D_2 (Yes/No), %	(3.1 / 96.9)	(3.2 / 96.8)	(2.3 / 97.7)	> .05*
D_3 (Yes/No), %	(5.3 / 94.7)	(4.7 / 95.3)	(11.6 / 88.4)	> .05*
D_4 (Yes/No), %	(14.0 / 86.0)	(14.2 / 85.8)	(11.6 / 88.4)	> .05*
D_5 (Yes/No), %	(.9 / 99.1)	(.8 / 99.2)	(2.3 / 97.7)	> .05**
D_6 (Yes/No), %	(10.2 / 89.8)	(10.7 / 89.3)	(4.7 / 95.3)	> .05*
D_7 (Yes/No), %	(.7 / 99.3)	(.8 / 99.2)	(.0 / 100)	> .05**

D_1 = Ciclosporin + Cellcept + Prednisolone
D_2 = Ciclosporin + Tacrolimus + Prednisolone
D_3 = Ciclosporin + Azaram + Prednisolone
D_4 = Cellcept + Tacrolimus + Prednisolone
D_5 = Azaram + Prednisolone + Sirolimus
D_6 = Cellcept + Prednisolone+ Sirolimus
D_7 = Ciclosporin + Prednisolone + Sirolimus
† independent t-test
*Chi-Square Tests
**Fisher's Exact Test

Table 2. The Relationship Between Each Immunosuppressive Drug and Risk of Malignancy

		Malignancy						*P*
		Yes		No		Total		
		Count	%	Count	%	Count	%	
Prednisolone	No	0	0.0	12	2.4	12	2.2	> .05
	Yes	43	100.0	494	97.6	537	97.8	
Cellcept	No	7	16.3	60	11.9	67	12.2	> .05
	Yes	36	83.7	446	88.1	482	87.8	
Tacrolimus	No	37	86.0	418	82.6	455	82.9	> .05
	Yes	6	14.0	88	17.4	94	17.1	
Azathioprine	No	37	86.0	478	94.5	515	93.8	< .05
	Yes	6	14.0	28	5.5	34	6.2	
Sirolimus	No	40	93.0	444	87.7	484	88.2	> .05
	Yes	3	7.0	62	12.3	65	11.8	
Ciclosporin	No	8	18.6	140	27.7	148	27.0	> .05
	Yes	35	81.4	366	72.3	401	73.0	

Table 3. Classification of Post-transplant Malignancies by Recipient's Gender, and Age

		Total No 43 (%)	Gender of Recipient No (Male/Female)	Recipient Age (years)	Recipient Age at Transplant (years)
NMSC (32%)	SCC_scalp	1 (2.3)	1/0	69.00	59.00
	SCC_nose	2 (4.7)	0/2	72.00	53.00 ± 9.90
	SCC_penis	1 (2.3)	1/0	77.00	60.00
	SCC_face	1 (2.3)	0/1	69.00	52.00
	SCC_sternom	1 (2.3)	0/1	73.00	61.00
	SCC_of thigh	1 (2.3)	1/0	33.00	29.00
	BCC_face	3 (7.0)	1/2	52.50 ± 14.85	34.00 ± 11.27
	BCC_scalp	1 (2.3)	1/0	55.00	37.00
	BCC_sternom	1 (2.3)	0/1	67.00	61.00
	BCC_nose	1 (2.3)	0/1	50.00	30.00
	BCC_of forehead	1 (2.3)	1/0	49.00	30.00
Kaposi Sarcoma		9 (20.9)	6/3	66.63 ± 10.21	54.22 ± 12.46
Total SKIN Cancers		23 (53.5)	12/11	62.60 ± 12.70	48.48 ± 14.02
	Small Intestine	1 (2.3)	0/1	55.00	37.00
	Colorectal	3 (7.0)	2/1	63.67 ± 17.04	52.00 ± 22.65
	Stomach	3 (7.0)	3/0	65.50 ± 3.54	53.33 ± 7.64
	esophagus	1 (2.3)	0/1	55.00	43.00
Total Gastrointestinal Cancers		8 (18.6)	5/3	61.71 ± 10.98	49.50 ± 14.16
	Multiple Myeloma	1 (2.3)	1/0	48.00	35.00
	B-cell Lymphomas	4 (9.3)	3/1	45.00 ± 11.53	35.67 ± 6.03
	Lynpho-proliferative with Plasmocytoid Feature	1 (2.3)	1/0	45.00	37.00
Total Lynphoproliferative		6 (14.0)	5/1	46.17 ± 7.52	36.50 ± 4.23
	Scc of Lung	1 (2.3)	1/0	76.00	65.00
	Small Cell Carcinoma of Lung	1 (2.3)	1/0	48.00	40.00
Total Lung Cancers		2 (4.7)	2/0	62.00 ± 19.80	52.50 ± 17.68
Genital	Breast	1 (2.3)	0/1	63.00	47.00
Urinary	Prostate	1 (2.3)	1/0	68.00	60.00
Brain	Brain	1 (2.3)	0/1	75.00	58.00
Heart	Heart	1 (2.3)	0/1	38.00	29.00
Total Number of Cancers		43 (100)	24/19	59.72 ± 13.13	47.19 ± 13.42

SCC, squamous cell carcinoma; BCC, basal cell carcinoma

enhancing role in PTM (Table 4).

The prevalence of malignancies in kidney transplant recipients are 26.9 times the prevalence of it in Guilan province (95% CI: 19.7 to 35.9) and 21.7 times higher than its prevalence in the country (95% CI: 15.9 to 28.9). In this study, the prevalence of all malignancies in kidney transplant recipients are 792 per 100000 person year (Table 5). A total of 549 subjects were followed by 5426 persons-years (mean follow-up time of 10 years, minimum 6 months and maximum 20 years), of which 43 cases of cancer were recorded. The incidence of cancer was estimated at 79.2 per 10,000 people per year (95% CI: 58.8 to 106.8). Table 5 shows the estimated cancer risk adjustment for each of the variables. As mentioned earlier, the age of patient at the time of transplantation was significantly associated with an increased risk of cancer, With each one year increase in age the risk of cancer increased by 4% (95% CI: 1.01 to 1.09, $P < .05$). The highest risk of cancer with 266 per 10,000 people per year was observed in the age group over 60 years at the time of transplantation and then in the age group of 50 to 60 years($P < .05$) (Table 6). Figure shows the survival function until the onset of cancer by age groups.

DISCUSSION

Numerous studies have been conducted to investigate the incidence of various malignancies and its related risk factors in KTR. Many of these studies have reported a higher incidence of malignancy in KTR compared to gender and age matched general population.[9] Also it is mentioned that malignancy is one of the major causes of death after cardiac and infectious diseases in this group of patients.[4] Beyond the first year of transplantation, therefore, mortality due to malignancy in KTR is 8 to 10% in the USA and more than 30% in Australia.[4]

The high risk of malignancy in the post-transplant

Table 4. Multivariate Logistic Regression Analysis for Risk Factors for Post-transplant Malignancies

Characteristics	OR	95% CI		*P*
		Lower	Upper	
Recipient Age at Transplant, y	1.038	1.014	1.063	< .05
Azathioprine (Yes/No)	2.968	1.136	7.759	> .05
Constant	0.015			

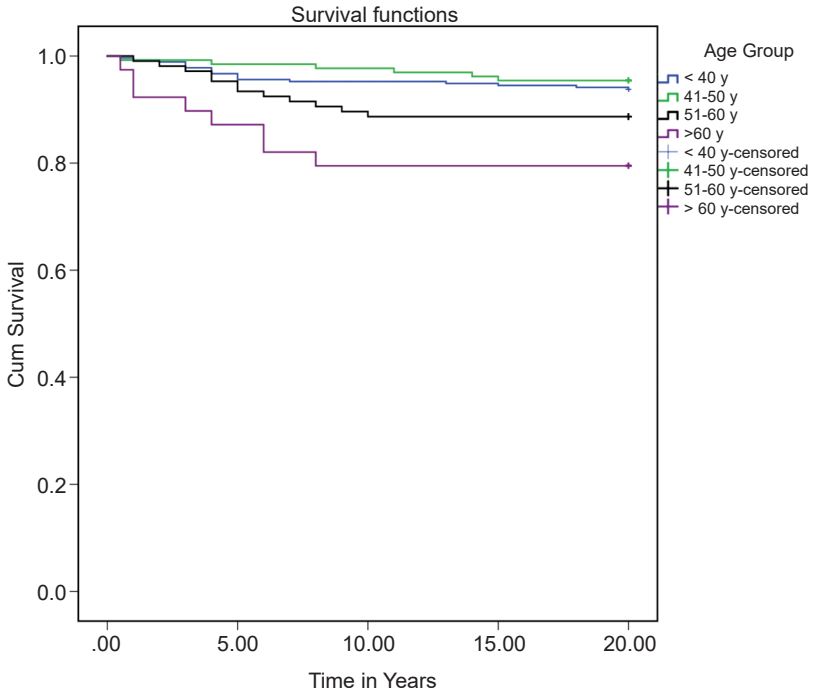
Table 5. Standardized Incidence Ratio (SIR) for Post-transplant Malignancies

Age Group	Provincial Incidence Rate per 100000	Expected Number of Cancer	National Incidence Rate per 100000	Expected Number of Cancer	Kidney Transplant Population	Observed Number of Cancer
15 to 19	4.9	0.00010	16.66	0.00033	2	0
20 to 24	13.2	0.00185	22.94	0.00321	14	0
25 to 29	29.4	0.00706	32.5	0.00780	24	0
30 to 34	40.9	0.01677	50.85	0.02085	41	2
35 to 39	117	0.06201	76.11	0.04034	53	1
40 to 44	114	0.06384	120.89	0.06770	56	1
45 to 49	243	0.17253	173.89	0.12346	71	9
50 to 54	301	0.19264	273.33	0.174931	64	3
55 to 59	452	0.32092	386.58	0.274472	71	3
60 to 64	457	0.26049	579.17	0.330127	57	5
65 to 69	387	0.17415	775.60	0.349020	45	9
70 to 74	439	0.11853	969.46	0.261754	27	4
75 to 79	708	0.1062	1255.50	0.188325	15	5
80 to 84	1226	0.08582	1575.29	0.110270	7	1
85 <	744	0.01488	1419.85	0.028397	2	0
Total		1.597781		1.980988	549	43

	SIR	95% CI	
		Lower	Upper
Study vs. Guilan	26.9	15.9	28.9
Study vs. Iran	21.7	19.7	35.9

Table 6. Adjusted Hazard Ratios for Cancer After Transplantation

Variables	Adjusted HR	95% CI		*P*
		Lower	Upper	
Recipient Age at Transplant, y	1.04	1.01	1.09	< .05
Gender of Recipient (Male)	1.78	0.79	4.02	> .05
Smoking (Yes/No)	1.33	0.35	4.99	> .05
Sun Exposure				
Low	1.00	Referent		
Moderate	0.90	0.26	3.08	> .05
High	0.30	0.50	1.70	> .05
Graft Status (Survival/Fail)	0.95	0.29	3.10	> .05



Kaplan–Meier plot for malignancy incidence after kidney transplantation in Guilan (between 1998 and 2018) stratified by age groups: (1) < 40 years; (2) 41 to 50 years; (3) 51 to 60 years, and (4) > 60 years.

period is largely related to the following:

1- Factors related to patients: age of the recipient, history of cancer, sun exposure, viral infection, and duration of dialysis.
2- Factors related to transplantation: risk of donor transmission, donor type and allograft rejection.
3- Factors related to medication: net immunosuppression, induction and maintenance therapy.[4]

In our study, there was no significant statistical relationship between patients' gender and malignancy. Whereas, some studies in the United States and Spain have reported that the male gender was a risk factor for post-transplant malignancy.[10,11] In these studies, men who received a kidney transplant were generally 20 to 30% more likely to develop a malignancy than women. Also in another study, female gender was a risk factor for malignancy after transplantation.[12] But the result of a study in Iran was Consistent with our result.[13] Given that the difference in race and geography of the place of residence can affect the incidence of malignancy, the similarity of the results of our study with that research, which was performed on recipients of transplantation with the same race and geographical area, can be justified.[13]

In this research, 7.7% of the total samples and 9.3% of patients with malignancy were current smokers, and no statistically significant relationship was observed between smoking and malignancy after transplantation. Whereas, in study by Danpanich *et al.* smoking has been reported as a common risk factor for malignancy after transplantation.[14] The

difference between the result of our study and the above research is justified by longer duration of their study (34 years vs. 20 years), smaller sample size and history of smoking cessation in our study.

Since total doses of immunosuppressive drugs are associated with higher risk of cancer, it is not surprising that patients with acute rejection receiving more anti-rejection medication have higher risk of developing cancer. Also doses of maintenance drugs such as CSA or tacrolimus, cellcept or azathioprine and/or steroids are often increased during the treatment of rejection, thus may contribute to increased T cell dysfunction.[15] Apart from T-cell dysfunction, systemic inflammation and release of cytokines and chemokines may be involved in transformation to malignany.[16]

Our study showed no statistically significant relationship between incidence of malignancy and use of ATG and Zenapax as induction therapy. But Lim and *et al* showed that taking drugs that suppressed T-cells increased the risk of non-Hodgkin's lymphoma by 30 to 80% compared to people who did not receive them.[17] Because increasing age in kidney transplant recipients has a proven effect on malignancy after transplantation, this difference may be due to the age difference between the two studies.

Maintenance immunosuppression is essential after kidney transplantation to prevent allograft rejection. Although the role of total immunosuppression in the development of malignancy has been suggested, the effects of various immunosuppressive drugs has not been established. The mechanisms by which immunosuppression cause cancer include: decreased immune surveillance of tumors, decreased antiviral responses resulting in a specific increase of virus induced tumors and possibly the direct carcinogenic effect of immunosuppressive drugs such as cyclosporine and azathioprine.[18]

Regarding to the use of diverse combination of drugs for maintenance therapy, and the role of each immunosuppressive agent to increase the risk of malignancy we have evaluated the effect of them as combination and the effect of each one separately.

In our study, only combination of cyclosporine, azathioprine, and prednisolone in the final logistic regression model remained. But there was no significant statistical association between them ($P > .05$). Other studies have shown a relationship between immunosuppressive regimen and malignancies after transplantation.[19,20] This difference may be due to limited access to cumulative dose and through level of immunosuppressive drugs. Evaluating the role of each drug separately, we have found that the use of azathioprine had significant correlation with the incidence of malignancy. Our explanation to this finding is that azathioprine as the earliest drug used in the maintenance therapy after transplantation was using for longer time by patients, also the role of increasing age in those patients should be mentioned (which has a significant role in the incidence of malignancy in our study). In present study, among 549 KTR, 78 (14.2%) deaths occurred, of which 20 (25.6%) were due to malignancy. In a study by Farrugia *et al.* 2085 (10.9%) deaths occurred, of which 375 (18%) were due to malignancy. According to the study, cancer was the most common cause of death after kidney transplantation.[21] And that study was conducted over a period of 11 years and the recipients of the kidneys were from different races. But in our study, the investigation time was longer (20 years), the statistical population was smaller, and all recipients were from the same race. These can be considered as causes of higher mortality in our study.

The overall incidence of PTM in our population was 7.8%. Non-Melanoma Skin Cancer (NMSC) (32.6%), and Kaposi sarcoma (20.9%) were most common form of skin cancer. 16.2% of total malignancies were SCC. Of the seven SCC cases, four occurred in areas exposed to sunlight, of which two were farmers (50%) and exposed to moderate and high sunlight. Sun exposure, actually is primary risk factor in development of skin cancer.[22] But in our study, no statistically significant relationship was reported between sun exposure and malignancy. In another study in Iran, nine patients had skin malignancy, 5 patients (55.55%) had Kaposi sarcoma, and 4 patients (44.44%) had NMSC. All NMSC lesions were limited to the head and neck area. Outdoor jobs were found in at least 50% of NMSC cases, and sun exposure was a risk factor for skin malignancies.[23] In our study, a significant number (70%) of patients with malignancy were exposed to moderate daily sunlight. Considering that the angle of sunlight in northern Iran is different from other areas, and on the other hand, the number of cloudy days in this region is more common, this

can be accompanied by a decrease in UV radiation. These factors can explain the different results of the present study. However, further studies in this geographical area are needed to examine the relationship between sunlight and the concomitant use of certain immunosuppressive drugs and the duration of immunosuppression. In another study in Ireland with the aim of determining the incidence of all cancers after kidney transplantation, the number of non-melanoma skin cancers in kidney transplant patients was 1% of all non-melanoma skin cancers in the general population during the study years.[24] The risk of developing SCC in patients with kidney transplantation increased 82-fold compared to normal populations. Male KTR were at-risk for invasive SCCs in sun-exposed areas such as the scalp and outer ear.[24] While in a study in Iran, the overall incidence of PTM was 2%.[13] That was four-fold less than our finding. Its reason may be related to the smaller population in our study and the possibility of reviewing and facilitating access to the results of pathology in the city of Rasht compared to that multicenter study. As well, the overall incidence of malignancy in a study in Japan was reported 10.3%,[25] which is closer to the result of our study. In this study, the mean age of the individuals at the time of transplantation was higher than our study (43 vs. to 40 years).

After skin cancer, the gastrointestinal malignancy with 18.6% and lymphoproliferative malignancy 14% are in the next rank. The reason for the more common gastrointestinal cancer in this study compare to lymphoproliferative disorder may be the higher prevalence of this type of cancer in these areas, even in the non- transplant population.[26] A few malignancies may be associated with malignancy such as EBV with PTLD - HPV-16 and 18 with cervical, vulvar, vaginal, anal, head and neck cancers - HHV-8 with Kaposi's sarcoma, multicentric Castleman disease, primary effusion lymphoma, multiple myeloma and HBV - HCV with hepatocellular carcinoma and HIV Merkel cell carcinoma.[5]

To measure the relative risk of cancer in transplant recipients compared with the general population, we calculated a standardized incidence ratio (SIR) (i.e., observed/expected cases). The relative risk of cancer in kidney transplant recipients is 26.9 times the malignancies in Guilan province (SIR = 26.9, 95% CI: 19.7 to 35.9) and 21.7 times the malignancies in Iran (SIR = 21.7, 95% CI: 15.9 to 28.9). The high SIR in our study could be related to the small size of the population. In similar studies in Iran, SIR was not calculated, so it is not possible to compare the values obtained with previous studies. But in a study conducted in the United States on 175732 recipients of solid organ transplantation, SIR for cancers was generally 2.1 higher than the normal population (SIR = 2.1, 95% CI: 2.06 to 2.14), and SIR of kidney transplant recipients was 6.7 (SIR = 6.7, 95% CI: 6.12 to 7.23).[27] In a study in Sweden, SIR for NMSC was reported 57.7 (95% CI: 51.00 to 65.11)[28] and for Finland 39.2% (95% CI: 29.29 to 51.43)[29]. However, due to the small size of our population, it was not possible to calculate SIR separately for each cancers.

Consistent with the pattern observed in the general population and other studies,[14,30] it appears that older KTR have a greater incidence for developing malignancy.

CONCLUSION

The results of the present study showed that malignancy after transplantation is one of the important causes of morbidity and mortality in transplant recipients. The most common malignancies in these people were non-melanoma skin cancer, Kaposi sarcoma and then GI malignancy. According to the information obtained in this study, regular periodic examinations of kidney transplant recipients for early detection of malignancy is important.

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CONFLICTS OF INTEREST

The authors have declared that no conflicts of interest exist.

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