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Risk of Cancer in Retransplants Compared to Primary Kidney Transplants in the United States

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Abstract

Recipients of kidney transplantation have elevated risk of developing cancer. There are limited data on cancer risk in recipients of kidney retransplantation.

We used data from the Transplant Cancer Match Study, which links the U.S. transplant registry with 15 cancer registries. Cancer incidence in recipients of kidney retransplantation and primary kidney transplants was compared utilizing Poisson regression, adjusting for demographic and medical characteristics.

We assessed 109,224 primary recipients and 6,621 retransplants. Compared to primary recipients, retransplants were younger (median age 40 vs. 46 years), had higher PRA, and more often received induction with polyclonal antibodies (43% vs. 25%). A total of 5,757 cancers were observed in primary recipients and 245 in retransplants. Overall cancer risk was similar in retransplants compared with primary recipients (incidence rate ratio [IRR] 1.06, 95%CI 0.93-1.20, adjusted for age, gender, race/ethnicity, PRA, and use of polyclonal induction). However, renal cell carcinoma (RCC) occurred in excess among retransplants (adjusted IRR 2.03, 95%CI 1.45-2.77), based on 514 cases in primary recipients and 43 cases in retransplants.

Overall cancer risk did not differ in retransplants compared to primary recipients. Increased risk of RCC may be explained by the presence of acquired cystic kidney disease, which is more likely to develop with additional time with kidney disease and time spent on dialysis waiting for retransplantation.

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Keywords

kidney retransplantation; cancer; immunosuppression

Introduction

Risk of cancer is elevated among recipients of solid organ transplants (1, 2, 3), including kidney transplants. In large part, this increased risk occurs because of immunosuppressive therapy used to prevent rejection. Some of the cancers for which risk is elevated are caused by infections (e.g., non-Hodgkin lymphoma, which is caused by Epstein-Barr virus). Among kidney recipients, risk is also increased for renal cell carcinoma (RCC), which often arises in one of the native kidneys.

Patients undergoing retransplantation after a failed first kidney transplant can be immunologically more challenging than primary kidney recipients, because they more often present with higher panel reactive antibody (PRA) levels, therefore placing them at higher risk for rejection (4, 5).

Nonetheless, due to significant progress in immunology over the last 2 decades leading to better prevention and treatment of acute rejection, more patients with failed transplants are acceptable to undergo retransplantation. In fact, between 1990 and 2007, the number of kidney retransplants doubled in the United States (6). Approximately 15% of the more than 100,000 patients currently on the U.S. waiting list for kidney transplantation already had a previous kidney transplant (7).

Although the positive association of cancer with kidney transplantation is established, little is known regarding cancer risk in recipients of kidney retransplantation. Prior exposure to immunosuppression and differences in immunologic status of recipients of kidney retransplantation could have an impact in the risk of cancer. For example, retransplantation may be associated with higher risk of cancer than seen in primary transplants due to more frequent use of polyclonal antibodies for induction, treatment of rejection, or prolonged exposure to immunosuppressants. On the other hand, because people who undergo retransplantation may be selected for certain characteristics (e.g., based on a younger age or favorable underlying medical condition), their cancer risk might be lower than seen in the group of primary kidney recipients.

Information regarding cancer risk following kidney retransplantation may lead to changes in patient care, perhaps related to counseling and surveillance. The goal of this study is to compare cancer risk in recipients of kidney retransplantation with risk in recipients of a primary kidney transplant.

Methods

We used data from the TCM Study, which has been described in detail elsewhere (www.transplantmatch.cancer.gov) (2). Briefly, the Scientific Registry of Transplant Recipients (SRTR) was linked to 15 state and regional cancer registries, together covering

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approximately 50% of U.S. kidney transplants during 1987-2009. The cancer registries cover the states of California, Colorado, Connecticut, Georgia, Hawaii, Illinois, Iowa, Michigan, New Jersey, New York, North Carolina, and Texas, as well as the Seattle-Puget Sound area of Washington State. The study was approved by the human subjects committees of the National Cancer Institute and, as required, by the participating cancer registries. The clinical and research activities being reported are consistent with the Principles of Istanbul as outlined in the "Declaration of Istanbul on Organ Trafficking and Transplant Tourism."

The TCM Study includes 121,223 kidney-only transplants with follow-up information on cancer from the cancer registries. All causes of CKD were included. We excluded 766 transplants in people with unknown race or race outside one of the four major groups, 7 transplants that were a fifth transplant or higher in sequence, 4301 transplants preceded by non-kidney transplants, and 304 transplants in people who had transplants within 180 days following a prior transplant. Following the exclusions, there remained 115,845 transplants.

We compared primary kidney transplants and kidney retransplants with respect to age and year at transplant, race/ethnicity, gender, type of transplant (living donor vs. deceased-donor), use of induction medications, and immunologic risk assessed by PRA. We evaluated dialysis vintage as the duration of dialysis treatment before kidney transplantation. For retransplants, dialysis vintage was the period of dialysis after failure of the preceding transplant until retransplant. We also calculated the total dialysis vintage, which was the sum of time on dialysis before the primary transplant and any retransplants. Because patients with more than one transplant are included multiple times, statistical comparisons of these characteristics of primary kidney transplants and retransplants were accomplished using generalized linear models.

All invasive cancers were identified using the linked cancer registry data and classified by the Surveillance Epidemiology, and End Results program "site recode with Kaposi sarcoma and mesothelioma" with minor modifications (2, 8). For both primary transplants and retransplants, follow-up started at the later of transplantation or start of cancer registry coverage, and ended at death, graft failure, retransplantation, loss to follow-up by the transplant registry, or end of cancer registry coverage, whichever occurred first. Cancer incidence was defined as the number of cancer cases observed divided by person-time at risk.

In statistical analyses of cancer risk, the transplant was considered the unit of analysis. We used Poisson regression to calculate unadjusted incidence rate ratios (IRR) comparing cancer risk following retransplant to risk among primary transplant recipients. Because many individual cancer types were uncommon, with few outcomes among retransplant recipients, we also created categories of cancer by organ system to achieve an acceptable number of cases that would permit age-adjusted analyses. In final multivariate models for cancer overall and RCC, we adjusted IRRs for demographic characteristics and factors that differed between the retransplants and primary transplants, specifically, age, gender, race/ethnicity, use of polyclonal antibody induction, and PRA. A p-value of <0.05 was considered statistically significant, although given the number of comparisons that we made, we emphasize associations with greater statistical significance.

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Results

We evaluated 109,224 primary kidney transplants and 6,621 kidney retransplants (6,309 second transplants, 296 third transplants, and 16 fourth transplants) in the U.S., followed between 1987 and 2009 (Table 1). Mean follow-up was 4.6, 3.7, 2.9, and 3.4 years for primary, second, third, and fourth transplants, respectively. More than 50% of primary transplants and more than 70% of the retransplants were performed between 2000 and 2009.

Compared with primary transplant recipients, retransplant recipients were substantially younger (median age at transplant 40 vs. 46 years), had a higher prevalence of glomerular disease, and a lower prevalence of diabetes mellitus and hypertension as the cause of chronic kidney disease (CKD). Compared to primary transplants, the percentage of non-Hispanic whites was higher in retransplants, while the percentage of racial/ethnic minorities was lower. Dialysis vintage immediately prior to transplantation was similar in primary transplant and retransplant recipients (median 645 vs. 731 days), but total dialysis vintage was longer for recipients of retransplantation (i.e., sum of time on dialysis before all prior transplants: median 1402 days).

Deceased donor kidneys were used more frequently in retransplantation (71%) than primary transplants (64%). PRA was higher in retransplants, and a larger fraction were highly sensitized (i.e., approximately 30% of retransplant patients had a PRA >80%, vs. 5% for primary transplants). More recipients of retransplants received a kidney from a 0 HLA mismatch donor (17%) compared to primary transplants (10%). Induction with polyclonal antibodies was employed more often in recipients of retransplantation (43%) compared to primary transplants (25%) (Table 1).

A total of 5,757 and 245 cancers were observed in recipients of primary transplants and retransplants, respectively (Table 2). Overall, cancer risk was lower in recipients of retransplantation (unadjusted incidence rate ratio [IRR] 0.87, 95%CI 0.77-0.99). Among specific cancer types, incidence was lower in recipients of retransplantation for cancers of the prostate (IRR 0.61, 95%CI 0.37-0.94), lung (IRR 0.65, 95%CI 0.4-0.98), colon and rectum (IRR 0.53, 95%CI 0.25-0.97), and breast (IRR 0.55, 95%CI 0.26-0.99), although these associations were of borderline significance. In contrast, only cancers of the kidney/renal pelvis showed significantly higher incidence in retransplants compared to primary transplants (IRR 1.61, 95%CI 1.19-2.12, p=0.0012). Most of these kidney cancers (80.5%) were RCCs, and as shown in Table 2, this excess risk in retransplantation was present specifically for RCC (IRR 1.72, 95%CI 1.24-2.31, p=0.0007).

These unadjusted IRRs partly reflect differences between primary transplants and retransplants shown in Table 1, especially the younger age of retransplants. Because many cancers were rare in recipients of a retransplant, we grouped cancers by organ/system to permit age-adjusted analysis. In these age-adjusted models (Table 3), retransplantation was no longer associated with a lower risk of cancer overall (IRR 1.06, 95%CI 0.93-1.20). As shown in Table 3, there were suggestive deficits of gastrointestinal tract and breast cancers, although these deficits were not significant. Notably, retransplantation was associated with higher risk of cancers of the kidney, renal pelvis, and bladder (age-adjusted IRR 1.74,

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95%CI 1.33-2.29). We also observed a higher risk for leukemias (age-adjusted IRR 2.30, 95%CI 1.05-5.02). All other age-adjusted analyses for cancers combined by organ/system did not yield statistical significance (Table 3).

In a multivariate model with adjustment for age as well as gender, race/ethnicity, use of polyclonal antibody induction, and PRA, recipients of a retransplant had a similar risk for cancer overall (IRR 1.06, 95% CI 0.93-1.20) but an elevated risk for RCC (IRR 2.03, 95%CI 1.45-2.77, $p<0.0001$), compared to recipients of a primary transplant. RCCs were diagnosed at similar stage in primary and retransplant recipients ($p=0.28$), with cancers presenting at localized stage in 78% and 90% of recipients, respectively. RCC grade distribution was also similar between both groups ($p=0.42$). Overall, retransplants had a longer time on dialysis before being diagnosed with RCC, as expected (total dialysis vintage including time on dialysis before primary transplant and before retransplant: median 1690 vs. 902 days). Nonetheless, retransplant recipients still had a higher risk of RCC than primary recipients after adjustment for age at transplant, gender, race/ethnicity, use of polyclonal induction therapy, PRA, and total dialysis vintage (IRR 1.81, 95%CI 1.29-2.47). Finally, when the time from most recent transplant to RCC diagnosis was examined, we observed a shorter interval for retransplants than primary transplants (median 790 vs. 1342 days, respectively.

Discussion

In this study, we demonstrated a similar overall risk of malignancy for recipients of kidney retransplantation compared to recipients of primary transplants. In unadjusted analyses, lower risk was apparent for several common cancers, including cancers of the lung, colorectum, prostate, and breast. However, these excesses were of marginal statistical significance, and some may have been due to differences between the retransplant and primary transplant groups. Importantly, after multivariate adjustment for demographic and clinical differences between retransplants and primary transplants, no difference in overall cancer risk was present. Notably, among all malignancies, only RCC was found at a higher incidence in retransplants.

As observed in our study, recipients of a retransplant have higher PRA than recipients of a primary transplant, and as a result of this greater sensitization, are more frequently treated with polyclonal antibody induction. In a recent publication by Lim et al. examining the impact of PRA on cancer outcomes in kidney transplantation, a higher risk of cancer was observed in patients with >80% PRA compared to 0% (9). Given a greater degree of immunosuppression, one might expect recipients of a retransplant to have a higher risk of cancer, particularly for cancers related to infectious causes such as anogenital cancers (caused by human papillomavirus [HPV]) and non-Hodgkin lymphoma (caused by Epstein-Barr virus). We did not observe that, however. Our findings differ from those in a recent publication by Madeleine et al. which, like our study, also used data from the TCM Study (10). They demonstrated a higher risk of anal and vulvar cancer for retransplants compared to primary transplants. The main difference from our study is that the previous cohort included all types of solid organ transplants, while our analysis focused only on kidney transplants. By restricting to one organ type, our comparison of cancer risk in retransplants and primary transplants may be less prone to bias. Nonetheless, the number of HPV-related

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cancers in our study was small, resulting in wide confidence intervals, so that we cannot rule out an increased risk associated with retransplantation.

In unadjusted analyses, we saw lower risk for some cancers in retransplants, which we attribute in large part to the younger age of retransplant recipients. A suggestion of lower risk of breast cancer and gastrointestinal tract cancers remained after adjustment for age, although the associations were no longer significant. After adjusting only for age, and in the final multivariate model adjusting for sex, age, race/ethnicity, use of polyclonal antibody induction, and PRA, the overall decreased risk of cancer was no longer apparent (both adjusted IRRs 1.06).

Kidney recipients have an almost 7-fold higher risk of kidney cancer than seen in the general population (2). In the present study, we demonstrate that recipients of retransplantation have a two-fold higher incidence of RCC than primary recipients (adjusted IRR 2.03). Recently, Wong et al. examined dialysis vintage and risk of cancer after transplantation in the ANZDATA registry, and found an association for urinary tract cancers (11). An elevated risk of RCC is present in patients with CKD, with further increase in risk as CKD advances (12), and risk is quite increased in patients on dialysis and among kidney transplant recipients (1, 2, 13).

Acquired cystic kidney disease (ACKD) is highly prevalent in patients with CKD. In ACKD, cysts originate in dilated renal tubules, and increase in number over time, even before the need for renal replacement therapy (14). After initiation of dialysis, the prevalence of cysts continues to increase, with the majority of patients having cysts after 10 years of dialysis, suggesting that the duration of CKD or dialysis is the main risk for development of renal cysts (15). ACKD is a risk factor for RCC (16), as RCCs can arise within these complex cysts (17). Prolonged dialysis and development of ACKD may partly explain the high risk of RCC in retransplant recipients, but unfortunately our study lacked data on the presence of ACKD.

Furthermore, even though retransplants in our study had a longer dialysis vintage than primary transplants, the excess risk of RCC was still present after we adjusted for dialysis vintage. Interestingly, recipients of retransplants had a shorter interval from transplant to RCC diagnosis compared to primary transplant recipients. This finding might suggest a more aggressive course of RCC after retransplantation, but whether there is a biological mechanism that explains this finding, or instead it reflects differences in duration of follow-up, is not known. Due to a higher risk for RCC in retransplants associated with a shorter interval from transplant to diagnosis, we compared grading and staging of RCC between both groups, but found no significant differences. A limitation of our study is that we could not determine that the RCCs that developed actually occurred in the diseased native kidneys, although we suspect that was the case for the majority (13).

In our age-adjusted analyses, we observed a higher risk for leukemias in retransplant recipients compared to primary kidney recipients. However, this increased risk was due to an excess of several types of leukemia. These malignancies likely do not all have the same

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etiology, but the small number of cases hindered a more detailed analysis. Given the rarity of leukemia, the clinical significance of this finding is uncertain.

This study has several strengths, including the availability of population-based data on transplant recipients and linkage to 15 cancer registries, which together cover almost half of all U.S. kidney transplants. This permitted inclusion of a large and representative population of kidney recipients and complete ascertainment of cancer outcomes. Also, our statistical adjustment allowed us to control for demographic and medical differences between the retransplants and primary recipients. Limitations include the lack of availability on some cancer risk factors (e.g., tobacco use) which may have confounded some analyses. Even though we made multiple comparisons in assessing risk for numerous cancers, the association with RCC was highly significant, arguing against chance as an explanation for that finding.

In conclusion, overall cancer risk is not increased among kidney retransplant recipients compared to primary kidney recipients, but the risk of RCC is elevated. Our findings should stimulate further investigation of RCC in retransplantation. It is likely that the majority of the RCC diagnoses occur in patients with pre-existing ACKD. Given the elevated risk of RCC, it may be beneficial to screen for this cancer in retransplant recipients, although a careful analysis of cost and benefits of screening should be conducted before implementing such an approach.

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List of abbreviations

CKD	Chronic Kidney Disease
IRR	Incidence Rate Ratio
PRA	Panel Reactive Antibodies
RCC	Renal Cell Carcinoma

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Table 1

Characteristics of U.S. Kidney Transplant Recipients

Characteristic		Primary Transplants (% of total)	Retransplants (% of total)	P-value
Calendar Year of Transplant	1987-1994	21,249 (19.45)	544 (8.22)	<.0001
	1995-1999	27,559 (25.23)	1,303 (19.68)	
	2000-2004	33,486 (30.66)	2,466 (37.25)	
	2005-2009	26,930 (24.66)	2,308 (34.86)	
Sex	Male	65,225 (59.72)	3,790 (57.24)	<.0001
	Female	43,999 (40.28)	2,831 (42.76)	
Age at Transplant, years	0-17	6,338 (5.80)	417 (6.30)	<.0001
	18-34	21,538 (19.72)	1,997 (30.16)	
	35-49	34,981 (32.03)	2,462 (37.18)	
	50-64	35,839 (32.81)	1,509 (22.79)	
	65+	10,528 (9.64)	236 (3.56)	
Reason For Transplant	Glomerular Disease	31,643 (28.97)	2,848 (43.01)	<.0001
	Diabetes	18,176 (16.64)	488 (7.37)	
	Polycystic Kidneys	9,815 (8.99)	439 (6.63)	
	Hypertension	18,623 (17.05)	820 (12.38)	
	Vascular Disease	4,348 (3.98)	221 (3.34)	
	Congenital/Rare Disorders	3,392 (3.11)	414 (6.25)	
	Tubular/Interstitial Disease	5,727 (5.24)	516 (7.79)	
	Other/Unknown	17,500 (16.02)	875 (13.22)	
Race/Ethnicity	White, Non-Hispanic	58,153 (53.24)	3,960 (59.81)	
	Black, Non-Hispanic	24,562 (22.49)	1,365 (20.62)	
	Hispanic	19,064 (17.45)	1,018 (15.38)	
	Asian/Pacific Islander	7,445 (6.82)	278 (4.20)	
Dialysis Vintage (Days)	0 – 244	26,030 (23.83)	1,492 (22.53)	<.0001
	245 – 650	25,872 (23.69)	1,546 (23.35)	
	651 – 1316	25,815 (23.63)	1,663 (25.12)	
	1317+	25,550 (23.39)	1,905 (28.77)	
	Missing	5,957 (5.45)	15 (0.23)	
Total Dialysis Vintage(Days)	0 - 244	26,028 (23.83)	424 (6.40)	<.0001
	245 - 650	25,872 (23.69)	923 (13.94)	
	651 - 1316	27,121 (24.83)	1,536 (23.20)	
	1317+	24,246 (22.20)	3,042 (45.94)	
	Missing	5,957 (5.45)	696 (10.51)	
Donor Type	Deceased	69,458 (63.59)	4,679 (70.67)	<.0001
	Living	39,766 (36.41)	1,942 (29.33)	
HLA Mismatch	0	11,452 (10.48)	1,133 (17.11)	<.0001
	1-2	18,882 (17.29)	1,183 (17.87)	
	3-4	45,005 (41.20)	2,499 (37.74)	
	5-6	32,805 (30.03)	1,775 (26.81)	

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Characteristic		Primary Transplants (% of total)	Retransplants (% of total)	P-value
	Missing	1,080 (0.99)	31 (0.47)	
PRA	0	51,506 (47.16)	1,255 (18.95)	<.0001
	1-79	50,073 (45.84)	3,328 (50.26)	
	80+	5,776 (5.29)	1,978 (29.87)	
	Missing	1,869 (1.71)	60 (0.91)	
Induction Therapy	Polyclonal antibody	27,459 (25.14)	2,867 (43.30)	<.0001
	Monoclonal antibody (OKT3)	6,287 (5.76)	393 (5.94)	0.5399
	Anti-IL2R	24,493 (22.42)	1,286 (19.42)	<.0001

Abbreviations: PRA panel reactive antibody, Anti-IL2R interleukin- 2 receptor antibody

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Table 2

Cancer Risk in Recipients of Primary Kidney Transplants and Retransplants

	Primary Transplant		Retransplant				
Cancer Type	**Cases**	**Incidence Rate**	**Cases**	**Incidence Rate**	**Unadjusted Incidence Rate Ratio**	**Lower 95% CI**	**Upper 95% CI**
Lip	82	16.2	2	8.1	0.50	0.08	1.58
Salivary Gland	32	6.3	3	12.2	1.92	0.46	5.37
HPV-Related Oropharynx	41	8.1	2	8.1	1.00	0.16	3.25
Other Oral Cavity and Pharynx	64	12.6	6	24.3	1.92	0.74	4.09
Nasopharynx	6	1.2	0	0	0	–	–
Esophagus	53	10.5	1	4.1	0.39	0.02	1.76
Stomach	98	19.4	0	0	0	–	–
Small Intestine	19	3.8	2	8.1	2.16	0.34	7.43
Colon and Rectum	346	68.4	9	36.5	0.53	0.25	0.97
Anus	49	9.7	3	12.2	1.26	0.31	3.42
Liver	53	10.5	0	0	0	–	–
Intrahepatic Bile Duct	6	1.2	0	0	0	–	–
Gallbladder	7	1.4	0	0	0	–	–
Other Biliary	15	3.0	0	0	0	–	–
Pancreas	98	19.4	5	20.3	1.05	0.37	2.32
Larynx	47	9.3	1	4.1	0.44	0.02	1.99
Lung	634	125	20	81.0	0.65	0.40	0.98
Bones and Joints	8	1.6	1	4.1	2.56	0.14	14.0
Soft Tissue including Heart	36	7.1	2	8.1	1.14	0.19	3.73
Melanoma of the Skin	270	53.3	11	44.6	0.84	0.43	1.45
Other Non-Epithelial Skin	117	23.1	8	32.4	1.40	0.63	2.69
Breast	338	66.8	9	36.5	0.55	0.26	0.99
Cervix	28	13.5	0	0	0	–	–
Uterus	72	34.6	4	37.1	1.14	0.35	2.75
Ovary	29	13.9	0	0	0	–	–
Vagina	8	3.8	1	9.3	2.56	0.14	14.0
Vulva	35	16.8	4	37.1	2.34	0.70	5.87

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	Primary Transplant		Retransplant				
Cancer Type	**Cases**	**Incidence Rate**	**Cases**	**Incidence Rate**	**Unadjusted Incidence Rate Ratio**	**Lower 95% CI**	**Upper 95% CI**
Prostate	637	214	19	137	0.61	0.37	0.94
Testis	30	10.1	1	7.2	0.68	0.04	3.19
Penis	14	4.7	1	7.2	1.46	0.08	7.29
Urinary Bladder	150	29.6	6	24.3	0.82	0.32	1.70
Kidney and Renal Pelvis	638	126	50	203	1.61	1.19	2.12
Kidney	621	123	50	203	1.65	1.22	2.18
RCC	514	102	43	174	1.72	1.24	2.31
Renal Pelvis	17	3.4	0	0	0	–	–
Eye and Orbit	15	3.0	1	4.1	1.37	0.08	6.74
Brain	39	7.7	0	0	0	–	–
Thyroid	175	34.6	8	32.4	0.94	0.42	1.78
Hodgkin Lymphoma	52	10.3	1	4.1	0.39	0.02	1.79
Non-Hodgkin Lymphoma	728	144	27	109	0.76	0.51	1.09
Myeloma	74	14.6	4	16.2	1.11	0.34	2.67
Acute Lymphoid Leukemia	6	1.2	1	4.1	3.42	0.18	20.0
Chronic Lymphocytic Leukemia	16	3.2	0	0	0	–	–
Acute Myeloid Leukemia	38	7.5	4	16.2	2.16	0.65	5.37
Chronic Myeloid Leukemia	20	4.0	1	4.1	1.03	0.06	4.92
Acute Monocytic Leukemia	2	0.4	0	0	0	–	–
Other Acute Leukemia	3	0.6	1	4.1	6.84	0.34	53.4
Mesothelioma	11	2.2	1	4.1	1.86	0.10	9.59
Kaposi Sarcoma	76	15.0	1	4.1	0.27	0.02	1.22
Miscellaneous	342	67.6	21	85.1	1.26	0.79	1.91
Tumors with Poorly Specified Morphology	101	20.0	3	12.2	0.61	0.15	1.62
All Cancers	5758	1137	245	993	0.87	0.77	0.99

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Table 3

Age-adjusted associations comparing cancer risk in primary kidney transplant and kidney retransplant recipients

	Primary transplant		Retransplant				
Organ system	**Cases**	**Incidence Rate**	**Cases**	**Incidence Rate**	**Incidence Rate Ratio**	**Lower 95% CI**	**Upper 95% CI**
Lip, Oral Cavity, Pharynx	225	44.4	13	52.7	1.35	0.77	2.37
Gastrointestinal Tract	565	112	15	60.8	0.72	0.43	1.20
Liver, Biliary Tract, and Pancreas	179	35.4	5	20.3	0.77	0.32	1.88
Lung	634	125	20	81.0	0.93	0.59	1.45
Bone and Soft Tissues	44	8.7	3	12.2	1.65	0.51	5.32
Melanoma and Other Skin	387	76.5	19	77.0	1.26	0.79	2.00
Breast	338	66.8	9	36.4	0.64	0.33	1.24
Female Reproductive	172	82.6	9	83.4	1.05	0.54	2.06
Male Reproductive	681	229	21	151	0.90	0.58	1.39
Kidney, Renal Pelvis, and Bladder	788	156	56	227	1.74	1.33	2.29
Thyroid	175	34.6	8	32.4	1.01	0.50	2.06
Lymphoid Neoplasms	869	172	32	130	0.77	0.54	1.09
Leukemias	69	13.6	7	28.4	2.30	1.05	5.02
Miscellaneous	631	125	28	113	1.14	0.78	1.67
All cancers	5,757	1137	245	992	1.06	0.93	1.20

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