Increased Risk of Post-Transplant Malignancy and Mortality in Transplant Tourists

A Nationwide Population-Based Cohort Study in Taiwan

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Abstract: Information on post-transplant malignancy and mortality risk in kidney transplant tourists remains controversial and is an important concern. The present study aimed to evaluate the incidence of post-transplant malignancy and mortality risk between tourists and domestic transplant recipients using the claims data from Taiwan’s universal health insurance.

A retrospective study was performed on 2394 tourists and 1956 domestic recipients. Post-transplant malignancy and mortality were defined from the catastrophic illness patient registry by using the International Classification of Diseases, 9th Revision. Cox proportional hazard regression and Kaplan–Meier curves were used for the analyses.

The incidence for post-transplant de novo malignancy in the tourist group was 1.8-fold higher than that of the domestic group (21.8 vs 12.1 per 1000 person-years). The overall cancer recurrence rate was approximately 11%. The top 3 post-transplant malignancies, in decreasing order, were urinary tract, kidney, and liver cancers, regardless of the recipient type. Compared with domestic recipients, there was a significantly higher mortality rate in transplant tourists (adjusted hazard ratio = 1.2, 95% confidence interval: 1.0–1.5). In addition, those with either pre-transplant or post-transplant malignancies were associated with increased mortality risk.

We suggest that a sufficient waiting period for patients with pre-transplant malignancies should be better emphasized to eliminate recurrence, and transplant tourists should be discouraged because of the possibility of higher post-transplant de novo malignancy occurrence and mortality.

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INTRODUCTION

In 2008, the Declaration of Istanbul stated that all transplant-related organizations should “prevent organ traffic.” Given the high prevalence of end-stage renal disease (ESRD) in Taiwan and the relative shortage of organ donors, numerous patients receive overseas commercial kidney transplants annually (these patients are known as transplant tourists). The Taiwanese government disapproves this behavior, but transplant tourists are still granted a catastrophic illness card and, without discrimination, are provided the same medical care as the patients who have domestically received kidney transplants (domestic kidney recipients). Patients with catastrophic illness certifications, who obtain care for their illness or related conditions within the certificate’s validity period, do not need to pay the copayment for outpatient or inpatient care (http://www.nhi.gov.tw).

In terms of patient and graft survival, previous studies in Taiwan and other countries reported that transplant tourists have similar or inferior outcomes compared with domestic recipients. However, no studies on pre-transplant and post-transplant malignancy occurrence, comparing transplant tourists with domestic recipients, have been conducted, except for 1 study conducted by a medical center in Taiwan. The present study was the largest study so far and based on a retrospective cohort study from a nationwide database. The purpose of this study was to determine the following: the incidence rates of pre-transplant and post-transplant malignancy in tourist and domestic kidney recipients; patient and graft survival in tourist and domestic kidney recipients; and the effects of malignancy occurrence prior to and after kidney transplant on prognosis.
METHODS

Data Source

We used the catastrophic illness patient registry and the inpatient database from the National Health Insurance Research Database (NHIRD). The NHIRD, which was established by the Taiwan Bureau of National Health Insurance (TBNHI) from the National Health Insurance Program, covers more than 99% of Taiwan residents. This database contains insurance information and medical claims of all 23 million insured individuals in Taiwan registered from 1996 to 2010. Disease diagnosis included details of medical orders, procedures, and medical diagnoses with codes based on the International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) in NHIRD. Because patients applying for the catastrophic illness card are exempt from cost sharing, most patients with catastrophic illness apply for this card, including patients with cancer and those undergoing dialysis and renal transplantation. This arrangement could indirectly increase the validity of disease diagnoses in our analysis. Insurant identification was encrypted before the information was sent to the researcher. This study was approved by the Institutional Review Board, China Medical University Hospital, Taiwan (CMU-REC-101–012). Details of NHIRD are shown on the TBNHI web page (http://w3.nhri.org.tw/nhird/date_01.html).

Study Subjects

Patients with new kidney transplants (ICD-9-CM V42.0 or 996.81) between 1999 and 2009 were included in this study (N = 4507). In addition, diagnoses in kidney recipients were validated according to the Registry for Catastrophic Illness Patient card. We excluded patients aged <18 years (n = 121) and those who had multiple kidney transplants (n = 36). A total of 4350 patients were selected and divided into tourist and domestic groups according to the ICD-9-CM procedure code 55.69, which indicated that the subjects underwent the kidney transplant surgery in Taiwan. Patients with ICD-9-CM 55.69 and had applied for the catastrophic illness card were defined as the domestic group. In contrast, those who applied for the catastrophic illness card but without ICD-9-CM 55.69 were defined as the tourist group. The entry date of the kidney transplant in our analysis was defined as the date of the application for inclusion in the Registry for Catastrophic Illness Patients.

Outcome Variables

The outcomes included the development of post-transplant malignancy (ICD-9-CM V42.0–208), graft failure (recurrent ESRD, ICD-9-CM 585), and all-cause mortality. Outcome variables of post-transplant malignancy and graft failure were based on primary discharge diagnosis, application for the catastrophic illness card, and confirmation of these events with at least 3 medical visits to increase the validity of the diagnoses. All study subjects were followed up from the entry date until the occurrence of each event, loss to follow-up date, or the end of 2010.

Covariate Assessment

The tested variables included age, gender, occupation, geographic location, and comorbidity. Occupation was divided into 3 groups (white collar, blue collar, and other) according to the workplace. Geographic locations were classified into 4 regions (northern, central, southern, and eastern) based on the subject’s residence. Comorbidity included diabetes (ICD-9-CM 250), hypertension (ICD-9-CM 401–405), coronary artery disease (CAD; ICD-9-CM 410–414), cerebrovascular disease (CVD; ICD-9-CM 430–438), pre-transplant malignancy history, hepatitis B viral infection (HBV; ICD-9-CM V02.61, 070.20, 070.22, 070.30, and 070.32), and hepatitis C viral infection (HCV; ICD-9-CM V02.62, 070.41, 070.44, 040.51, and 070.54). All comorbidities were defined before the entry date and were confirmed with at least 3 medical visits.

Statistical Analysis

The SAS 9.3 software for Windows (SAS Institute, Cary, NC) was used for all analyses, and the significance level was set to 0.05 in the 2-tailed test. χ2 and t tests were used to examine the differences in the distribution and the mean age, respectively, between the 2 groups. Mortality after kidney transplant, incidence of post-transplant malignancy, and recurrent ESRD per 1000 person-years were assessed in the 2 groups. The hazard ratios (HRs) and 95% confidence intervals (CIs) for the risk of malignancy and mortality were estimated using Cox proportional hazard regressions. Kaplan–Meier analysis was used to plot the disease-free rate and the cumulative incidence rate curve. The log-rank test was used to determine the difference between the 2 groups.

RESULTS

Comparison of Demographic Profiles of the Tourist and Domestic Groups

In total, 2394 and 1956 subjects were included in the analyses as tourist and domestic groups, respectively. Compared with the domestic group, the tourist group included more men (55.1% vs 48.4%) and was older (48.4 vs 42.7 years of age) (Table 1). More transplant tourist than domestic kidney recipients lived in the central and southern areas. The tourist group had more comorbidities than the domestic group, and the top 3 comorbidities were hypertension, diabetes, and CAD.

Incidence and Risk of Post-Transplant Malignancy

The mean follow-up durations were 5.6 and 5.2 years in the tourist and domestic groups, respectively. The incidence of post-transplant malignancy in the tourist group was 1.8-fold higher than that in the domestic group (21.8 vs 12.1 per 1000 person-years, Table 2). The Kaplan–Meier survival analysis during a 12-year follow-up period revealed that transplant tourists had significantly higher rates of post-transplant malignancy than domestic kidney recipients (log-rank P < 0.0001, Figure 1).

Pathology and Follow-Up Duration of Post- Transplant and Pre-Transplant Malignancies

A categorization of post-transplant and pre-transplant malignancies in the renal transplant group is presented in Table 3. The top 5 pre-transplant malignancies in the tourist group were urinary tract (25.0%), kidney (17.2%), liver (12.5%), breast (10.9%), and hematologic (9.4%) cancers, whereas malignancies in the domestic group included the kidney (25.8%), breast (22.6%), urinary tract (19.4%), thyroid (12.9%), head and neck (6.5%), and multiple (6.5%) cancers.
The top 5 post-transplant malignancies in the tourist group were urinary tract (33.5%), kidney (22.9%), liver (14.3%), colorectal (4.4%), and lung (4.4%) cancers, whereas malignancies in the domestic group included urinary tract (43.4%), kidney (13.9%), liver (9.8%), hematologic (5.7%), and breast (4.1%) cancers. The time from pre-transplant malignancy diagnosis to transplantation was shorter in the transplant tourist group than in the domestic recipient group (2.5 vs 3.8 years, \( P < 0.0001 \)). Most tourist and domestic kidney recipients developed post-transplant malignancies within 2 to 5 years (Table 4), and the 2 groups had similar mean follow-up times (3.68 vs 3.56 years).

### Types and Time Relationship of Kidney Transplants for Recurrent Malignancies

Urinary tract cancer was the most common among the 10 recurrent cancers. Six cancers occurred in the transplant tourists

### Table 1. Demographic Profiles of the Tourist and Domestic Groups

|                          | Tourist Group N = 2394 | Domestic Group N = 1956 | \( P \) Value |
|--------------------------|------------------------|-------------------------|--------------|
| Male                     | 1320                   | 946                     | <0.0001      |
| Age at transplantation, y|                        |                         |              |
| 18–40                    | 534                    | 779                     | <0.0001      |
| 40–65                    | 1723                   | 1149                    |              |
| >65+                     | 137                    | 28                      | 1.43         |
| Mean (SD)                | 48.4 (11.1)            | 42.7 (11.0)             | <0.0001      |
| Occupation               |                        |                         | 0.06         |
| White collar             | 779                    | 698                     | 35.7         |
| Blue collar              | 794                    | 642                     | 32.8         |
| Other                    | 821                    | 616                     | 31.5         |
| Geographic region        |                        |                         | <0.0001      |
| Northern                 | 1048                   | 1065                    | 54.5         |
| Central                  | 592                    | 350                     | 17.9         |
| Southern                 | 583                    | 395                     | 20.2         |
| Eastern                  | 171                    | 146                     | 7.5          |
| Comorbidity              |                        |                         |              |
| Diabetic                 | 428                    | 192                     | 9.8          | <0.0001      |
| Hypertension             | 1600                   | 1151                    | 58.8         | <0.0001      |
| CAD                      | 251                    | 132                     | 6.8          | <0.0001      |
| CVD                      | 122                    | 72                      | 3.7          | 0.02         |
| Hepatitis B              | 120                    | 61                      | 3.1          | 0.002        |
| Hepatitis C              | 64                     | 41                      | 2.1          | 0.22         |
| Pretransplant malignancy | 64                     | 31                      | 1.6          | 0.01         |

CAD = coronary artery disease, CVD = cerebrovascular disease, SD = standard deviation.

The top 5 post-transplant malignancies in the tourist group were urinary tract (33.5%), kidney (22.9%), liver (14.3%), colorectal (4.4%), and lung (4.4%) cancers, whereas malignancies in the domestic group included urinary tract (43.4%), kidney (13.9%), liver (9.8%), hematologic (5.7%), and breast (4.1%) cancers. The time from pre-transplant malignancy diagnosis to transplantation was shorter in the transplant tourist group than in the domestic recipient group (2.5 vs 3.8 years, \( P = 0.042 \)). Most tourist and domestic kidney recipients developed post-transplant malignancies within 2 to 5 years (Table 4), and the 2 groups had similar mean follow-up times (3.68 vs 3.56 years).

### Table 2. Incidence Rate and Hazard Ratios of Post-Transplant Malignancy Stratified by Follow-Up Years

| Malignancy Incidence | Tourism Group | Domestic Group | Tourism vs Domestic Group |
|----------------------|---------------|----------------|---------------------------|
|                      | N             | Person-Years | Rate                      | N             | Person-Years | Rate                      | Adjusted HR (95% CI) |
| Overall              | 293           | 13,446       | 21.8                      | 122           | 10,123       | 12.1                      | 1.8 (1.5–2.2)**      |
| <1 y                 | 40            | 2327         | 17.2                      | 13            | 1922         | 6.8                       | 2.5 (1.4–4.8)**
| <2 y                 | 89            | 4501         | 19.8                      | 37            | 3673         | 10.1                      | 2.0 (1.3–2.9)**
| 2–5 y                | 122           | 5155         | 23.7                      | 53            | 3802         | 11.9                      | 1.7 (1.2–2.3)**
| >5 y                 | 82            | 3790         | 21.6                      | 32            | 2647         | 12.1                      | 1.8 (1.2–2.7)**
| De novo cancer\(1\) | 279           | 13,165       | 21.2                      | 115           | 10,013       | 11.5                      | 1.9 (1.5–2.3)**
| Secondary cancer\(1\) | 8            | 281          | 28.4                      | 3             | 109          | 27.4                      | 1.0 (0.3–3.9)
| Recurrent cancer\(1\) | 6            | 281          | 21.3                      | 4             | 109          | 36.5                      | 0.6 (0.2–2.1)

CI = confidence interval, HR = hazard ratio, IRR = incidence rate ratio. Adjusted for age, gender, geographic region, and hypertension. *\( P < 0.05 \), **\( P < 0.01 \), ***\( P < 0.001 \). \(1\)De novo cancer: pre-transplant malignancy (–). \(2\)Secondary cancer: pre-transplant malignancy (+); other new type of post-transplant malignancy. \(3\)Recurrent cancer: pre-transplant malignancy (+); the same type of post-transplant malignancy.
and the other 4 occurred in the domestic kidney recipients. The 10 cancers included 5 urinary tract cancers, 3 kidney cancers, 1 breast cancer, and 1 thyroid cancer. Four of the recurrent cancers occurred within a waiting period of 1 year, and 6 occurred within 2 years (data not shown).

### Mortality and Risk of Death

The median follow-up durations were 6.0 and 5.0 years in the tourist and domestic groups, respectively. Kaplan–Meier survival analysis revealed that the transplant tourists had significantly worse survival than the domestic kidney recipients ($log-rank P < 0.0001$, Figure 2A). Furthermore, the mortality risk between the 2 groups was statistically significant after age, gender, geographic location, diabetes, CAD, HBV, stroke, renal transplant group, and pre-transplant malignancy were controlled ($log-rank P < 0.05$, Model 1; Table 5). Compared with the subjects without pre-transplant and post-transplant malignancies, the mortality risks were increased in those with pretransplant and post-transplant malignancies and in those with both malignancies after age, gender, geographic region, diabetes, CAD, HBV, stroke, and tourist/domestic group were controlled (Model 2). We further stratified the subjects with post-transplant malignancies by cancer type to investigate the association between malignancy and mortality risk. Patients with post-transplant liver cancer had significantly higher mortality risk than those without liver cancer ($HR = 7.0$.

![FIGURE 1. Cumulative incidence rates of overall post-transplant malignancy for the tourist (solid line) and domestic (dashed line) groups.](image)

### TABLE 3. Pathology of Overall Pre-Transplant and Post-Transplant Malignancy of Renal Transplant Recipients From 1999 to 2009

| Pathology (ICD-9-CM) | Pre-Transplant Malignancy | Post-Transplant Malignancy |
|----------------------|--------------------------|---------------------------|
|                      | Tourist Group (n = 64)   | Domestic Group (n = 31)   | Tourist Group (n = 293) | Domestic Group (n = 122) |
|                      | Number (%)               | Number (%)                | Number (%)              | Number (%)               |
| Head neck cancer (140–149) | 2 (3.1)                 | 2 (6.5)                   | 8 (2.7)                 | 3 (2.5)                  |
| Esophagus (150)       | 2 (0.7)                  | 1 (0.8)                   | 6 (2.1)                 | 0 (0.0)                  |
| Stomach (151)         | 1 (1.6)                  | 2 (3.2)                   | 13 (4.4)                | 1 (0.8)                  |
| Colorectal (153 and 154) | 8 (12.5)              | 0 (0.0)                   | 42 (14.3)               | 12 (9.8)                 |
| Liver (155)           | 1 (1.6)                  | 0 (0.0)                   | 2 (0.7)                 | 2 (1.6)                  |
| Gallbladder (156)     | 0 (0.0)                  | 2 (1.6)                   | 0 (0.0)                 | 2 (1.6)                  |
| Pancreas (157)        | 1 (1.6)                  | 0 (0.0)                   | 13 (4.4)                | 7 (5.7)                  |
| Peritoneum (158)      | 4 (1.4)                  | 1 (0.8)                   | 2 (0.7)                 | 1 (0.8)                  |
| Lung (162)            | 7 (10.9)                 | 7 (22.6)                  | 10 (3.4)                | 5 (4.1)                  |
| Bone, connective, and other soft tissues (170 and 171) | 3 (4.9) | 0 (0.0) | 1 (0.3) | 1 (0.8) |
| Melanoma and skin (172 and 173) | 0 (0.0) | 1 (0.8) | 0 (0.0) | 1 (0.8) |
| Breast (174 and 175)  | 16 (25.0)                | 6 (19.4)                  | 98 (33.5)               | 53 (43.4)                |
| Kaposi’s sarcoma (176) | 11 (17.2)             | 8 (25.8)                  | 67 (22.9)               | 17 (13.9)                |
| Cervix (180)          | 5 (1.7)                  | 1 (0.8)                   | 7 (2.4)                 | 5 (4.1)                  |
| Endometrial (182)     | 0 (0.0)                  | 1 (0.8)                   | 1 (0.3)                 | 0 (0.0)                  |
| Vagina (184)          | 1 (1.6)                  | 0 (0.0)                   | 2 (0.7)                 | 2 (1.6)                  |
| Prostate (185)        | 6 (9.4)                  | 0 (0.0)                   | 8 (2.7)                 | 7 (5.7)                  |
| Urinary tract (188, 189.1–189.9) | 1 (1.6) | 4 (12.9) | 5 (1.3) | 0 (0.0) |
| Kidney (189.0)        | 5 (7.8)                  | 2 (6.5)                   | 8 (2.7)                 | 7 (5.7)                  |

ICD-9-CM = International Classification of Diseases 9th Revision; Clinical Modification.
DISCUSSION

This study involves the largest cohort in the investigation of transplant tourists. Compared with domestic kidney recipients, transplant tourists showed a significantly higher post-transplant de novo malignancy incidence and mortality risk. The occurrence of malignancy both prior to and after transplant was associated with worse patient survival.

In the present analyses, transplant tourists were significantly older and had higher prevalence rates of diabetes mellitus, hypertension, CAD, CVD, HBV, and even pre-transplant malignancies. This result might be attributed to 2 factors. First, according to the scoring system of receiving deceased donor renal transplants in Taiwan (http://www.torsc.org.tw/assize/assizeWaitKidney.jsp), older patients with more comorbidities might think that they had lower priority to receive deceased renal transplants and seek kidney transplant abroad. Second, we found that transplant tourists with pre-transplant malignancy had a significantly shorter waiting period compared with domestic kidney recipients (2.5 vs 3.8 years, P < 0.05), which indicates that transplant tourists opted to receive kidney transplants abroad to avoid the long waiting period.

A higher percentage of transplant tourists lived in central and southern areas of Taiwan, and a higher percentage of domestic recipients lived in the northern area. A total of 27 hospitals support kidney transplant in Taiwan, 12 and 8 of which are located in the northern and central areas, respectively. Six hospitals are in the southern area, and only 1 is in the eastern area. This geographic difference between the tourist and domestic recipients may be because of the unequal medical resources in Taiwan.

Kidney transplantation itself is a significant risk for post-transplant malignancy. The types of post-transplant malignancy in Taiwan differ from those in Western countries.14–16 In our findings, tourist and domestic recipients exhibited similar types of post-transplant malignancies. Urinary tract cancer was the most common in both recipients, followed by kidney and liver cancers. However, this ranking was different from the results described by Li et al14 who reported that kidney cancer, not urinary tract cancer, is the most common type of malignancy. This difference may be attributed to the exclusive criteria of patients for pre-transplant malignancy recruitment and duration during kidney transplant to post-transplant malignancy in their study. Additionally, other studies in Taiwan have shown that urinary tract cancer develops more frequently than kidney cancer.17,18 which is consistent with our study.

Previous studies have reported prevalence rates of 1.7% to 3.6% for pre-transplant malignancy in kidney recipients.20–22 In our study, the prevalence rates of pre-transplant malignancy were 2.7% and 1.6% in tourist and domestic kidney recipients, respectively. For the total of 95 pre-transplant malignancies, the overall cancer recurrence rate was 11% (10 recurrent cancers). High recurrence rates of 19% (4/21) and 15.4% (6/39) were noted for waiting periods of 1 and 2 years, respectively, which suggests that a waiting period that is >2 years could eliminate 60% of recurrent cancer incidence (6/10). Therefore, patients should be clearly educated on this issue to prevent hasty kidney transplants.

Previous studies have reported post-transplant malignancy-related risk factors such as old age, male gender, and history of cancer.23 After adjusting for these factors, the transplant tourists

95% CI = 4.9–10.0, Model 3). Similar results were also observed in other cancer types. In addition, no significantly increased risk of graft failure was observed in either the transplant tourist or domestic kidney-recipient groups (P = 0.45, data not shown).

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Previous studies have reported post-transplant malignancy-related risk factors such as old age, male gender, and history of cancer.23 After adjusting for these factors, the transplant tourists
might lead to underestimation on their mortality or graft failure. 
nonfunction kidney graft after transplants abroad, both of which 
transplant malignancy in the present study, all of which might 
previous meta-analysis, and transplant tourists had more post-
vival. Based on our analysis, patients with pre-transplant or/and 
post-transplant lymphoproliferative disorder had the worst sur-
status and poor medical care of tourist donors might result in 
more unknown malignancies and lead to donor-derived malign-
ancy to recipients. We inferred that the poor socioeconomic 
costs. This action is reflected in the similar follow-up times 
apply for the catastrophic illness card to reduce their medical 
ment of these 2 groups was ensured.

The present study showed that transplant tourists had 
inferior patient survival compared with domestic kidney recip-
ients despite the same quality of post-transplant medical care 
available for both groups in Taiwan. High rates of infectious and 
surgical complications were observed in transplant tourists in 
previous meta-analysis, and transplant tourists had more post-
transplant malignancy in the present study, all of which might result in higher patient mortality. Notably, we could not esti-
mate how much transplant tourists died shortly or had primary 
nonfunction kidney graft after transplants abroad, both of which 
might lead to underestimation on their mortality or graft failure. 

Reulen et al reported a significantly higher long-term mortality rate for cancer survivors compared with the general 
population. Death caused by post-transplant malignancy in kidney transplant recipients has gradually increased in recent 
years. Pedotti et al reported significantly poorer 10-year survival with post-transplant malignancy, and patients with 
post-transplant lymphoproliferative disorder had the worst sur-
vival. Based on our analysis, patients with pre-transplant or/post-transplant malignancies had significantly increased 
mortality risks. In particular, patients with liver cancer as their 
post-transplant malignancy had the worst prognosis.

The limitations of this study are as follows. First, we could 
not distinguish living related from deceased kidney transplants 
from our database, which may affect the mortality risk to a 
certain extent. Second, no detailed information regarding cancer 
pathologic types, staging, or treatment was available, which 
may also affect mortality risk. Third, we could not consider all 
possible confounders, such as smoking, analgesic usage, Chi-
nese herb usage, and decreased hydration, which have been 
related to urinary tract cancer. Fourth, no detailed information 
on the immunosuppressant use was available, which may be 
associated with malignancy occurrence, especially mammalian 
 target of rapamycin (mTOR) inhibitor. However, a previous 
 study conducted in Taiwan has shown that only minority of 
 kidney transplant recipients use inhibitors of the mammalian 
target of rapamycin (mTOR) inhibitor. However, a previous 

| TABLE 5. Adjusted Hazard Ratio by Cox Proportional Hazard Model of Effect of Tourist Group, Pre-Transplant and Post-Transplant Malignancy (Overall/Different Types) on Patient Mortality |
|-----------------|-----------------|-----------------|-----------------|-----------------|
|                  |                | Crude           | Adjusted        |
| **Model 1: tourism group vs domestic group** |                  |                |                |
| Pre-transplant malignancy | Post-transplant malignancy |                |                |
| No               | No             | 1.6 (1.4–2.0)*** | 1.2 (1.0–1.5)*  |
| No               | Yes            | 3.4 (2.8–4.1)*** | 2.9 (2.4–3.5)***|
| Yes              | No             | 3.8 (2.3–6.3)*** | 3.4 (2.0–5.8)***|
| Yes              | Yes            | 2.3 (1.2–4.3)*  | 2.0 (1.1–3.8)*  |
| **Model 2: interaction of pre-transplant and post-transplant malignancy** |                  |                |                |
| Pre-transplant malignancy | Post-transplant malignancy |                |                |
| No               | No             | 1.0             | 1.0             |
| No               | Yes            | 5.9 (1.5–23.8)* | 5.6 (1.4–22.9)* |
| Yes              | No             | 4.3 (2.1–9.1)*** | 3.7 (1.7–7.8)**  |
| Yes              | Yes            | 4.3 (2.5–7.3)**  | 2.3 (1.3–4.0)**  |
| **Model 3: people with post-transplant malignancy** |                  |                |                |
| Liver cancer (155) |                  | 7.0 (4.9–10.0)*** | 5.8 (4.0–8.4)*** |
| Gynecological cancer (180–184) |                  | 5.9 (1.5–23.8)* | 5.6 (1.4–22.9)* |
| Post-transplant lymphoproliferative disorder (200–209) |                  | 4.3 (2.1–9.1)*** | 3.7 (1.7–7.8)**  |
| Gastrointestinal carcinoma (150–154, 156–159) |                  | 4.3 (2.5–7.3)**  | 2.3 (1.3–4.0)**  |
| Kidney cancer (189.0) |                  | 2.7 (1.8–4.1)*** | 2.7 (1.8–4.0)*** |
| Urinary tract (188, 189.1–189.9) |                  | 2.3 (1.6–3.2)*** | 2.3 (1.6–3.2)*** |
| Breast cancer (174–175) |                  | 2.4 (0.9–6.5)    | 2.7 (1.0–7.3)*  |
| Other            |                  | 4.1 (2.7–6.1)*** | 2.7 (1.8–4.1)*** |

Model 1: adjusted for age, gender, geographic region, diabetes, CAD, HBV, stroke, renal transplant group and pre-transplant malignancy. Model 2: adjusted for age, gender, geographic region, diabetes, CAD, HBV, stroke, and renal transplant group. Interaction P for pre-transplant and post-
transplant malignancy was 0.007 in adjusted model. Model 3: adjusted for age, gender, geographic region, diabetes, CAD, HBV, stroke, and renal transplant group in patients without pre-transplant malignancy. P < 0.05. * P < 0.01. ** P < 0.001. CAD = coronary artery disease, HBV = hepatitis B viral infection.
malignancy surveillance prior to and after kidney transplant is required, and hospitals should place more emphasis on a sufficient waiting period. The most important thing is transplant tourists should be discouraged because of the possibility of higher post-transplant de novo malignancy occurrence and mortality.

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