Editorial

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Approach to kidney transplant patients with pre-transplant malignancy

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History of pre-transplant malignancy prior to kidney transplantation has long been considered a relative contraindication for kidney transplant due to the belief that immunosuppression after transplantation would promote malignancy recurrence. There are four major issues of concern about the effects of pre-transplant malignancy on kidney transplant recipients: recurrence of primary tumors, increase of *de novo* malignancy, adverse effects on patient survival, and graft-specific outcomes such as rejection.

Ban et al [1] recently analyzed 3,748 patients in two Korean transplantation centers and indicated that the frequency of pre-transplant malignancy increased, and type of the malignancy changed because of introduction and dissemination of a national cancer screening system. They also reported that pre-transplant malignancy did not affect either primary tumor recurrence or *de novo* malignancy after kidney transplantation. Based on the results, additional discussion on pre-transplant malignancies is expected because the topic has been relatively neglected compared to other clinical issues in Korea. This study is the first to present data on pre-transplant malignancy in Korea. However, there were some limitations because the study included a relatively small number of patients and data from only two clinical centers in Korea. Therefore, careful interpretation is needed to apply these results to actual clinical practice because a variety of different outcomes have been reported on the impact of pre-transplant malignancy on post-transplant outcomes [2–7].

Most guidelines recommend that patients with a history of pre-transplant malignancy wait to receive a kidney transplant for a minimum defined time after successful treatment because of the risk of recurrence [8]. In addition, the guidelines also suggest advising patients with prior malignancy of the increased risk of *de novo* malignancy compared with patients that do not have a previous history of malignancy that undergo transplantation. Previous reports have indicated that kidney transplant recipients with a history of pre-transplant malignancy showed higher incidence of post-transplant *de novo* malignancies and higher recurrence rate after kidney transplantation [2]. However, there are limited data available to provide guidance on the suitability for performing transplants in patients with a prior malignancy, as most information has been drawn from research on Western population-based databases [3–7]. Table 1 summarizes the reported literature on clinical outcomes of transplant patients with a previous cancer [1,3–7]. However, the results are controversial, and recent studies that focus on cancer risk in kidney graft recipients with pre-transplant malignancy do not help address questions that arise in everyday clinical practice.

The reason for recommending a waiting period in patients with a history of pre-transplant malignancy is because of previous assertions that risk of post-transplant

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Table 1. Literature review of kidney transplant outcomes for recipients with a history of pre-transplant malignancy

Author (year)	Population	Number in cohort	Summary of results	Ref.
Webster et al (2007)	Australia and New Zealand	15,183	HR 1.4 for *de novo* malignancies vs. patients without a previous cancer history; variable according to race and age.	3
Brattström et al (2013)	Sweden	10,448	HR 1.3 for all causes mortality vs. patients without a previous cancer history	4
Farrugia et al (2014)	UK	19,103	Higher risk of death from malignancy compared to those without any previous history (17.6% vs. 1.9%)	5
Dahle et al (2017)	Norway	5,867	All-cause mortality - similar, but HR 1.97 for cancer-specific mortality vs. patients without a previous cancer history; higher in the first 5 years	6
Unterrainer et al (2019)	Collaborative Transplant Study registry	272,325	HR 1.7 for all post-transplant tumor vs. patients without a previous cancer history (higher recurrence and higher *de novo* malignancy) No relation between pre-transplant waiting time and cancer recurrence	7
Ban et al (2019)	Korea	3,748	Recurrence rate 4.2% in patients with a previous cancer history, *de novo* malignancy 6.9% in patients without pre-transplant malignancy	1

HR, hazard ratio.

tumor recurrence could depend on the length of the interval between pre-transplant tumor diagnosis and renal transplantation [2]. However, recent studies have not reported strong evidence to support recommendations that longer intervals between cancer diagnosis and renal transplantation decrease the risk of tumor recurrence [7].

As Ban et al [1] suggested in their paper, the incidence of pre-transplant malignancy has changed significantly over time, and treatment approaches have also advanced and changed. Over the last decade, thyroid cancer and renal cell carcinoma (RCC) were the most frequent pre-transplant malignancy cases in Korea. Considering that there was no recurrence after transplantation in these two types of pre-transplant malignancy, it is likely that separate criteria are needed for these common types of pre-transplant malignancy. Therefore, it has become clear that special criteria are needed for thyroid cancer, which tends to be diagnosed early in medical examination or incidentally discovered during parathyroidectomy in patients with end-stage renal disease. The current guidelines for RCC also suggest that no delay is required for subjects with small or incidentally discovered RCC, while the recommendations for patients who have been treated for symptomatic RCC or for those with large or invasive tumors are conflicting. In this issue of Journal, Park et al [9] also reported that patients with early-stage and asymptomatic RCC did not require a mandatory observational period prior to kidney transplantation after curative nephrectomy.

Most researchers have suggested that patients should be individually evaluated for risk of cancer recurrence after transplantation. However, there is currently no significant prediction model that can provide parameters for overall survival and cancer-specific survival in transplanted patients. The main limitations of these tools are that most systems for prediction of clinical prognosis have not been validated in transplant patients or in any other patient group that require immunosuppressive drugs for long periods of time. Some studies have suggested that the fixed waiting time for transplantation in patients with a history of pre-transplant malignancy is no longer justified [7,10]. To date, evidence suggests that superficial cancer in the bladder, cervix, and skin and asymptomatic T1 RCC do not require a waiting period for kidney transplantation, although some invasive tumors should be avoided because of a high risk of recurrence or metastasis after transplantation [8].

Based on current and emerging research, patients should be individually evaluated for risk of cancer recurrence, expected survival, and quality of life. The possibility of increased risk of developing *de novo* malignancy should be discussed with patients as well as physicians. However, in the context of rapidly developing diagnostic tools and treatment advancements in current clinical practice, further research and guidelines need to be developed for renal transplantation in patients with a history of pre-transplant malignancy.

Conflicts of interest

The author has no conflicts of interest to declare.

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