Trends and Outcomes with Kidney Failure from Antineoplastic Treatments and Urinary Tract Cancer in France

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Abstract

Background and objectives Cancer survival is improving along with an increase in the potential for adverse kidney effects from antineoplastic treatments or nephrectomy. We sought to describe recent trends in the incidence of kidney failure related to antineoplastic treatments and urinary tract cancers and evaluate patient survival and kidney transplantation access.

Design, setting, participants, & measurements We used the French Renal Epidemiology and Information Network registry to identify patients with kidney failure related to antineoplastic treatments or urinary tract cancer from 2003 to 2015. We identified 287 and 1157 cases with nephrotoxin- and urinary tract cancer–related kidney failure, respectively. The main study outcomes were death and kidney transplantation. After matching cases to two to ten controls (n=11,678) with other kidney failure causes for age, sex, year of dialysis initiation, and diabetes status, we estimated subdistribution hazard ratios (SHR) of each outcome separately for patients with and without active malignancy.

Results The mean age- and sex-adjusted incidence of nephrotoxin-related kidney failure was 0.43 (95% CI, 0.38 to 0.49) per million inhabitants and 1.80 (95% CI, 1.68 to 1.90) for urinary tract cancer–related kidney failure; they increased significantly by 5% and 2% annually, respectively, during 2006–2015. Compared with matched controls, age-, sex-, and comorbidity-adjusted SHRs for mortality in patients with nephrotoxin-related kidney failure were 4.2 (95% CI, 3.2 to 5.5) and 1.4 (95% CI, 1.0 to 2.0) for those with and without active malignancy, respectively; for those with urinary tract cancer, SHRs were 2.0 (95% CI, 1.7 to 2.2) and 1.1 (95% CI, 0.9 to 1.2). The corresponding SHRs for transplant wait-listing were 0.19 (95% CI, 0.11 to 0.32) and 0.62 (95% CI, 0.43 to 0.88) for nephrotoxin-related kidney failure cases and 0.28 (95% CI, 0.21 to 0.37) and 0.47 (95% CI, 0.36 to 0.60) for urinary tract cancer cases. Once on the waiting list, access to transplantation did not differ significantly between cases and controls.

Conclusions Cancer-related kidney failure is slowly but steadily increasing. Mortality does not appear to be increased among patients without active malignancy at dialysis start, but their access to kidney transplant remains limited.

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Introduction

Improvement in diagnosis and more effective treatments have resulted in substantially better cancer survival for all ages worldwide (1,2). In France, cancer incidence increased from 321 per 100,000 person-years in 1990 to 402 in 2005, but recent trends (2010–2018) indicate this rate dropped by 1% per year. In contrast, mortality has been steadily declining by 2% per year on average over the last 20 years (3,4). Survivors of cancer are, however, at risk of developing adverse effects caused by their oncologic treatments or surgery, which may affect the kidneys (5–7). Nephrotoxicity is a known side effect of radiotherapy and of several commonly used antineoplastic drug classes, which can cause glomerular or tubular dysfunction and impair kidney functions (8,9). The importance of overall nephrotoxin-related ESKD is currently unknown. Nephrectomy for urinary tract cancer, whether radical or partial, has also been associated with the onset of CKD (10) and ESKD (11–13).

Mortality associated with cancer-related ESKD has mainly been studied in patients with kidney cancer (11,13,14). Overall, survival of these patients on KRT is reported to be worse than that of those with other known ESKD causes (11,13). Furthermore, patients with cancer-related ESKD have tended to wait longer to be registered on the transplant waiting list—from 2 to 5 years longer, depending on the cancer type and

stage (14–17). An evaluation of cancer-related ESKD trends and outcomes in the context of improved cancer survival and broader access to dialysis and transplantation is needed.

We used data from the French Renal Epidemiology and Information Network (REIN) registry to describe trends in the incidence of cancer-related ESKD, whether due to nephrotoxins or to urinary tract cancer, and compare mortality and access to kidney transplantation between these patients and those with ESKD from other causes, while taking malignancy status (active or not) at dialysis initiation into account.

Materials and Methods

Patients

The French REIN registry includes all patients on KRT for ESKD, whether they are receiving dialysis or transplantation. The registry started in 2002 and expanded progressively to achieve nationwide coverage in 2012. Details of its methods and quality control have been reported elsewhere (18). This study includes all incident patients for whom the attending nephrologist reported chemotherapy, radiotherapy, or urinary tract cancers as the main or contributing cause of ESKD in the years 2002–2015 (Supplemental Table 1) and excludes those with ESKD related to hematologic malignancies or those who underwent preemptive transplantation.

In all, 1435 cases were identified, including 287 patients with nephrotoxin-related ESKD due to chemotherapy or radiation treatment and 1157 with urinary tract cancer–related ESKD (Figure 1). ESKD for nine of these patients was attributed to both causes. Patients with cancer-related ESKD were individually matched to two to ten patients with other causes of ESKD for sex, age (±5 years), year of dialysis initiation (±5 years), and diabetes status. Controls with active malignancy reported as a comorbidity at dialysis initiation were excluded to avoid any misclassification due to errors in assigning the cause of ESKD. A total of 11,748 control patients with ESKD were selected. The French data protection authority approved the data collection conducted by the REIN registry, and the REIN scientific committee approved the study.

Information

Baseline data were collected from patients' medical records by nephrologists or clinical research assistants. Three ESKD causes could be reported and were coded using the 10th revision of the International Classification of Disease (18). Biopsy-proven diagnoses were specifically reported. Other information included demographics, body mass index, comorbidities, mobility status (autonomous, partially or totally dependent), and dialysis start condition (planned or unplanned, *i.e.*, started on an emergency basis). Comorbidities included diabetes, chronic respiratory disease, the number of cardiovascular diseases (zero, one, two, three or more) among coronary artery disease, cerebrovascular disease, peripheral artery disease, heart failure, dysrhythmia, and active malignancy. REIN coding instructions call for patients to be classified as having an active malignancy at the initiation of KRT if they then had any type of cancer not in remission or if they had been treated for cancer or had metastases in the 2 years before KRT.

Outcomes

We studied mortality on maintenance dialysis in the overall population, as well as access to the national transplant waiting list and to kidney transplantation in patients <75 years, through December 31, 2015. For the first two outcomes, time to event was calculated from dialysis initiation. Time to kidney transplantation was calculated from wait-listing date, either before or after dialysis start, to avoid immortal time bias.

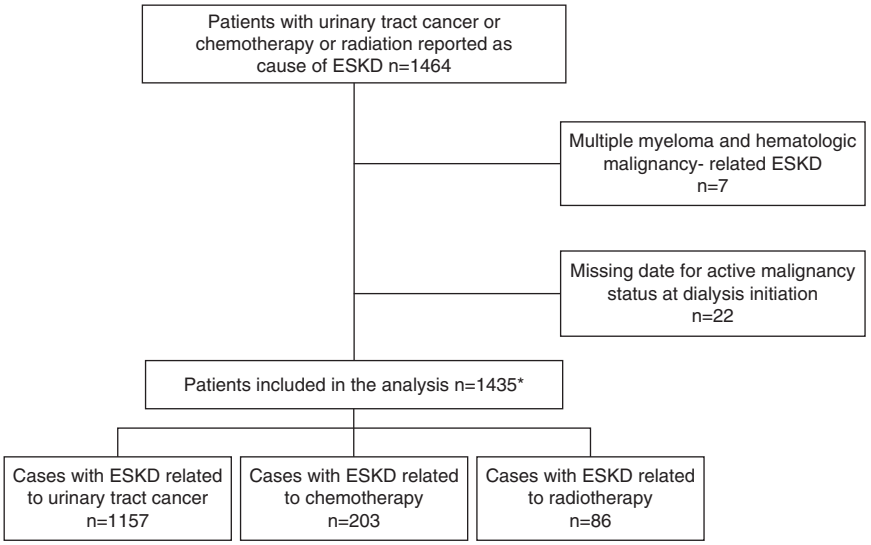

Figure 1. | **Study flow chart**.

Statistical Analyses

We calculated mean incidence rates of cancer-related ESKD, nephrotoxin-related ESKD, and urinary tract cancer–related ESKD per million inhabitants (pmi), overall, by sex and by age group (<44, 45–64, 65–74, ≥75 years) for the overall 2006–2015 period. We also calculated age- and sex-adjusted annual incidence rates of cancer-related ESKD and their 95% confidence intervals (CIs), overall and by subtype, from 2006 to 2015, standardized according to the French population as of June 30, 2015. Time trends in incidence rates over the 10-year period were tested for overall cancer-related ESKD and by subtype with Join-Point software (19).

We then used chi-squared or Mann–Whitney tests, as appropriate, to describe baseline patient characteristics and compared cases with nephrotoxin- and urinary tract cancer–related ESKD with their matched controls. Missing data for some variables led to the performance of multiple imputations of 20 data sets with the fully conditional specification method. Analyses of the 20 complete data sets were combined according to the Rubin rules (20).

We used cumulative incidence functions and the Fine and Gray competing-risk regression models to estimate and compare all-cause mortality as well as cancer and noncancer mortality risks of all cases and matched controls. The Gray test was used to compare cumulative incidence functions between groups (21).

Similarly, we estimated and compared transplant wait-listing and kidney transplantation rates for patients aged <75 years and their matched controls. Cumulative incidence rates were estimated separately for cases with and without active malignancy at baseline, given this condition's strong influence on prognosis and kidney transplant indication. The competing event in the mortality analysis was kidney transplantation; for the analyses of waiting list and kidney transplantation access, the competing event was death. Finally, for each subtype of cancer-related ESKD, we estimated subdistribution hazard ratios (SHRs) of death and their 95% CIs before and after adjustment for age, sex, diabetes status, cardiovascular comorbidities, liver disease, respiratory disease, and dialysis start condition. Similarly, we estimated SHRs of wait-listing and kidney transplantation before and after adjustment for age, sex, diabetes status, cardiovascular comorbidities, and temporary contraindication for transplantation. P values <0.05 were considered statistically significant, and all analyses were performed with SAS 9.4.

Results

Incidence of Cancer-Related ESKD

The mean incidence for overall cancer-related ESKD over the study period was 2.22 pmi (95% CI, 2.11 to 2.34). It significantly increased by 3% (95% CI, 0.6% to 5%) annually from 2006 to 2015 (Figure 2). The mean incidence of nephrotoxin-related ESKD was 0.43 pmi (95% CI, 0.38 to 0.49) with a significant annual increase of 5%; for urinary tract cancer–related ESKD, it was 1.80 pmi (95% CI, 1.68 to 1.90) with an annual increase of 2%. The incidence of urinary tract cancer–related ESKD was more than three times higher in men than women and increased strongly with age. (Supplemental Table 2). Nephrotoxin-related ESKD incidence was almost twice as high in men as in women and increased only slightly with age up to 65–74 years, but not afterward.

Patient Characteristics at Baseline

Among the 287 patients with nephrotoxin-related ESKD, ESKD was attributed to platinum-based chemotherapies for 59%. Among the 1157 patients with urinary tract cancer–related ESKD, 58% of these cases were related to renal cell carcinoma (Supplemental Table 1). Nephrectomy was reported as a contributing cause of ESKD in 50% of urinary tract cancer cases and only in 4% of nephrotoxin-related ESKD; non-neoplastic disease was reported in 34%

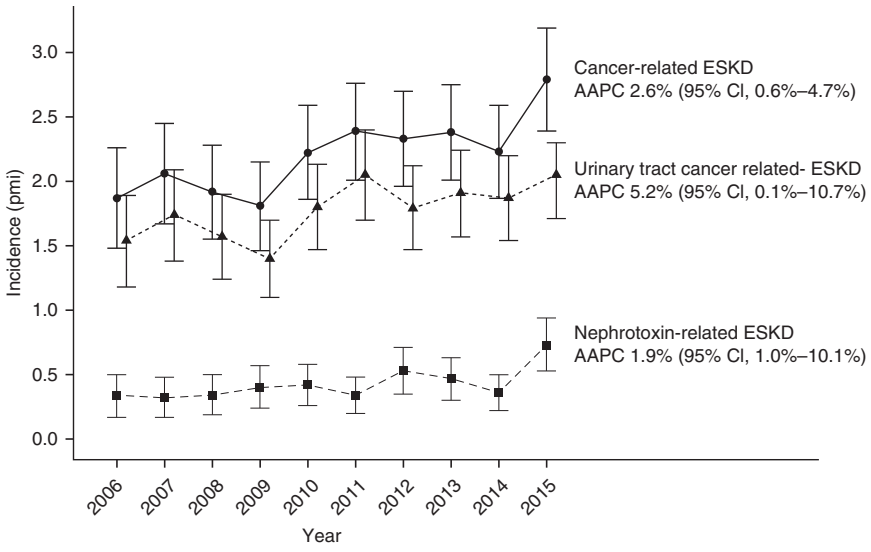

Figure 2. | Standardized incidence rates per million inhabitants (pmi) of cancer-related ESKD increased between 2006 and 2015. AAPC, average annual percent change; 95% CI, 95% confidence interval.

Table 1. Baseline characteristics of patients with nephrotoxin- or urinary tract cancer–related ESKD and matched controls at dialysis initiation

Characteristics	Nephrotoxin-Related ESKD		Urinary Tract Cancer–Related ESKD	
	Case Patients (n=287)	Matched Controls (n=2368)	Case Patients (n=1157)	Matched Controls (n=9380)
Median age, yr (range)[a]	65 (21–93)	65 (21–93)	73 (1–100)	73 (0–100)
Age in years, *n* (%)[a]				
<44	30 (10)	259 (11)	34 (3)	292 (3)
45–64	109 (38)	914 (39)	258 (22)	2132 (23)
65–74	95 (33)	738 (31)	337 (29)	2689 (29)
≥75	53 (19)	457 (19)	528 (46)	4267 (45)
Men, *n* (%)[a]	176 (61)	1439 (61)	882 (76)	7057 (75)
Year at dialysis start, *n* (%)[a]				
<2009	78 (27)	786 (33)	365 (32)	3137 (33)
2009–2012	106 (37)	864 (37)	431 (37)	3448 (37)
2013–2015	103 (36)	718 (30)	361 (31)	2795 (30)
Kidney biopsy, *n* (%)	42 (15)	554 (23)	113 (10)	1541 (16)
Diabetes, *n* (%)[a]	41 (14)	369 (16)	263 (23)	2275 (24)
Body mass index, *n* (%)				
<18.5 kg/m^2	34 (15)	113 (6)	50 (5)	361 (5)
18.5–24.9 kg/m^2	123 (53)	816 (45)	430 (43)	3276 (45)
25–29.9 kg/m^2	62 (26)	589 (32)	336 (34)	2389 (33)
≥30 kg/m^2	15 (6)	305 (17)	174 (18)	1250 (17)
Active malignancy, *n* (%)[b]	174 (61)	0	683 (59)	0
Respiratory disease, *n* (%)	33 (12)	238 (10)	148 (13)	1275 (14)
Cardiovascular disease, *n* (%)[c]				
0	159 (62)	1260 (57)	518 (53)	3690 (42)
1	62 (24)	476 (21)	217 (22)	2241 (26)
2	24 (9)	284 (13)	156 (16)	1536 (18)
≥3	12 (5)	204 (9)	84 (9)	1223 (14)
Liver disease, *n* (%)	2 (1)	75 (3)	11 (1)	204 (2)
Treatment modality, *n* (%)				
Hemodialysis	274 (95)	2090 (88)	1106 (96)	8243 (88)
Peritoneal dialysis	13 (5)	278 (12)	51 (4)	1137 (12)
Started emergency dialysis, *n* (%)	95 (33)	624 (26)	352 (30)	2559 (27)
Wait-listed for kidney transplantation at dialysis start, *n* (%)	12 (4)	340 (14)	16 (1)	664 (7)
Reasons for not being wait-listed, *n* (%)				
Medical contraindication	215 (75)	951 (40)	942 (81)	5227 (56)
Assessment in progress	25 (9)	547 (23)	45 (4)	1259 (13)
Patient refusal	1 (0)	32 (2)	5 (0)	96 (1)
Other	19 (7)	197 (8)	56 (5)	828 (9)
Unknown	27 (9)	641 (27)	109 (9)	1970 (21)

[a]Matching criteria.
[b]Active malignancy was an exclusion criterion among controls.
[c]Cardiovascular diseases included coronary heart disease, cerebrovascular disease, peripheral artery disease, heart failure, and dysrhythmia.

and 27%, respectively. The percentage of biopsy-proven diagnosis, however, was low in both groups (Table 1).

At dialysis initiation, around 60% of the patients in both subgroups had an active malignancy (Table1). Compared with their matched controls, patients with nephrotoxin- and urinary tract cancer–related ESKD had cardiovascular and liver disease significantly less often, were more likely to be treated with hemodialysis than peritoneal dialysis, and were less likely to be wait-listed for kidney transplantation.

Mortality on Dialysis

Median follow-up was 2.4 years (interquartile range [IQR], 0.9–4.3) and 3.6 years (IQR, 0.9–4.7) for nephrotoxin- and urinary tract cancer–related ESKD, respectively. In patients with nephrotoxin-related ESKD and without active malignancy at dialysis initiation, 2-year mortality was 29% versus 16% in controls and for those with active malignancy, 65% versus 21% (Figure 3A). The corresponding rates in patients with urinary tract cancer–related ESKD and active malignancy were 48% versus 26% in their controls, but were similar for patients without active malignancy and their controls (Figure 3B). The cumulative incidence of cancer versus noncancer mortality was higher in patients with active malignancy at baseline, regardless of the type of cancer-related ESKD (Table 2). In those without active malignancy at baseline, the cumulative incidence of cancer compared with noncancer mortality was much lower. However, it was still higher than in matched controls.

Adjusting for covariates did not substantially modify the SHRs for all-cause mortality estimated by the Fine and Gray models in any subgroup (Table 3).

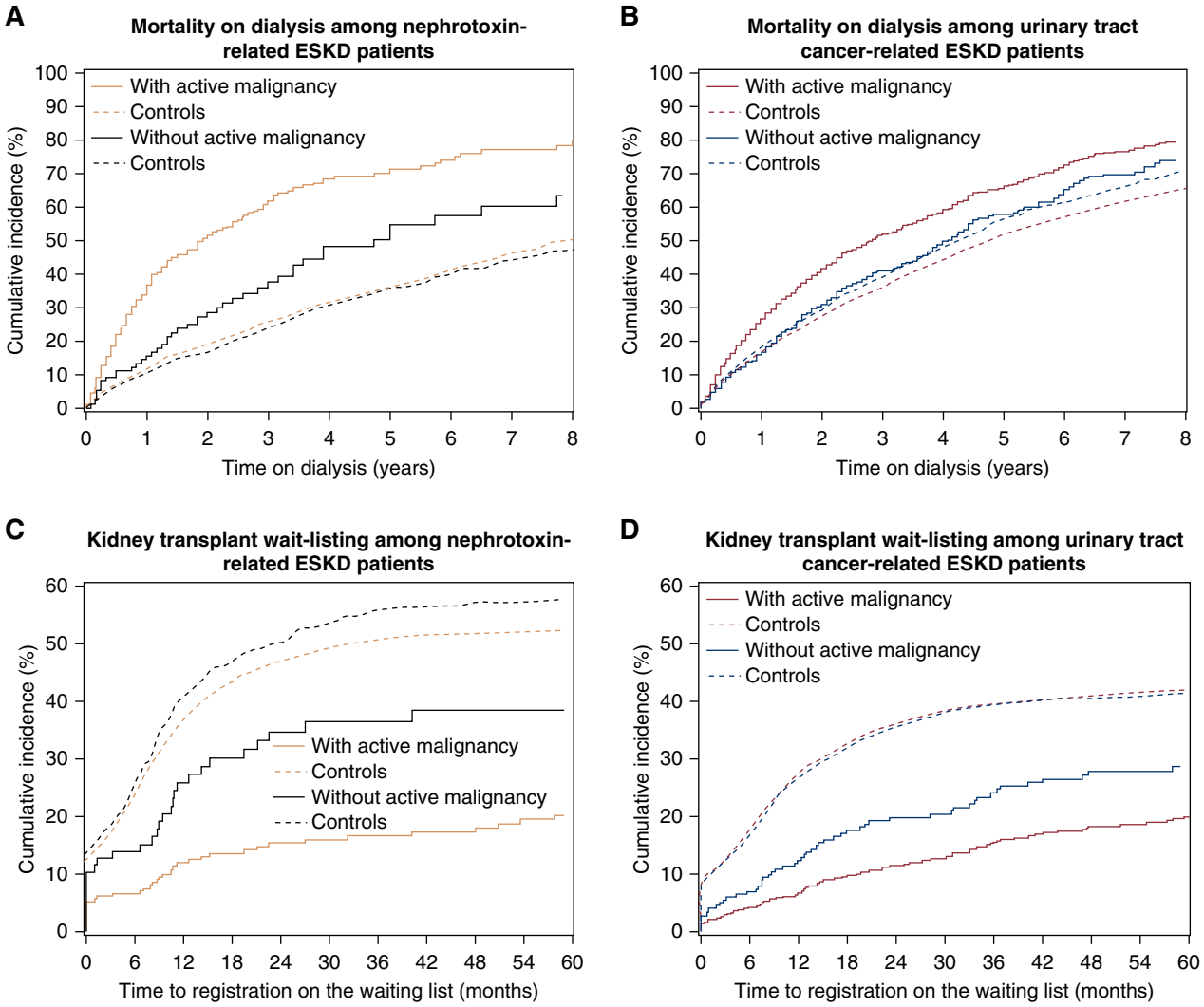

Figure 3. | **Cumulative incidence of all-cause mortality and wait-listing for kidney transplantation.** (A) Mortality on dialysis among patients with nephrotoxin-related ESKD. (B) Mortality on dialysis among patients with urinary tract cancer–related ESKD. (C) Kidney transplant wait-listing among patients with nephrotoxin-related ESKD. (D) Kidney transplant wait-listing among patients with urinary tract cancer–related ESKD.

Registration on the Waiting List for Kidney Transplantation

In all, 41 patients with nephrotoxin-related ESKD (18%) and 100 urinary tract cancer–related ESKD (16%) were wait-listed for kidney transplantation during the study period, together with 2855 controls (41%). Patients with nephrotoxin-related ESKD without active malignancy at dialysis initiation waited for a median time of 8.7 (IQR, 0–12.7) versus 6.7 months (IQR, 0–12.9) in controls ($P=0.05$), and those with active malignancy waited for 40.3 (IQR, 3.6–55.7) versus 6.3 months (IQR, 0–12.9) ($P=0.01$). Patients with urinary tract cancer–related ESKD without active malignancy waited a median of 12.8 (IQR, 4.5–31.0) versus 7.3 months (IQR, 0.7–15.1) for their controls ($P=0.01$), and those with active malignancy waited for 14.8 (IQR, 6.3–33.0) versus 6.8 months (IQR, 0.5–14.8) ($P<0.001$).

Of those patients with nephrotoxin-related ESKD, 34% of patients without an active malignancy, 50% of their controls, 4% of those with active malignancy, and 45% of their controls were wait-listed within 2 years (Figure 3C). For patients with urinary tract cancer–related ESKD, 19% of those without active malignancy, 36% of their controls, 7% of those with active malignancy, and 37% of their matched controls were wait-listed within 2 years. (Figure 3D) Adjusting for covariates did not substantially modify SHRs for wait-listing (Table 3).

Access to Kidney Transplantation

Once on the waiting list, neither the probability nor the timing of kidney transplantation differed significantly between patients with nephrotoxin- or urinary tract cancer–related ESKD compared with their matched controls, but the number of events was small. Of the patients with nephrotoxin-related ESKD, 55% with and 21% without active malignancy at dialysis start were transplanted within 12 months after being wait-listed, compared with 32% in both control groups. Among the patients with

Table 2. Mortality risk from malignancy and other causes in patients with nephrotoxin- and urinary tract cancer–related ESKD and their matched controls

Mortality Risk	Nephrotoxin-Related ESKD				Urinary Tract Cancer–Related ESKD			
	Controls	Patients with Active Malignancy	Patients without Active Malignancy	*P* Value[a]	Controls	Patients with Active Malignancy	Patients without Active Malignancy	*P* Value[a]
Mortality risk from malignancy (%)				<0.001				<0.001
1 yr	0.5	28	6		0.8	18	2	
2 yr	1	40	11		2	26	6	
Mortality risk from causes other than malignancy (%)				0.08				<0.001
1 yr	11	22	10		16	15	14	
2 yr	18	30	19		26	22	25	

[a]Mortality risks estimated by cumulative incidence functions were compared between the three groups using Gray's test.

urinary tract cancer–related ESKD, these percentages were 36% and 41% for patients with and without active malignancy and 32% and 38% for their respective controls (Supplemental Figure). In the multivariable models, the probability of transplantation did not differ significantly between cases and controls (Table 3).

Discussion

This registry-based study shows that cancer-related ESKD, notably nephrotoxin-related ESKD, has been slowly but steadily increasing over the past decade in the French population. As expected, survival among patients with active malignancy at dialysis initiation was very poor and their access to kidney transplantation limited. More unexpectedly, patients whose cancer had not been active in the 2 years before starting dialysis also experienced a much lower rate of wait-listing than matched controls with other causes of ESKD, despite similar survival on dialysis.

The incidence of KRT for ESKD continues to rise in most countries including France, mainly as a result of population aging, increasing diabetes prevalence, and extended dialysis access criteria (22). However, the annual increases of 5% for nephrotoxin-related ESKD and 2% for urinary tract cancer–related ESKD far exceeded the 0.8% annual increase estimated for the overall French ESKD population over this period (23). These findings highlight the growing importance of cancer-related ESKD, which we may have underestimated due to the lack of coding for ESKD causes related to more novel anticancer agents such as vascular endothelial growth factor, EGF receptor pathway inhibitors, targeted therapies, and immunotherapy (6,9).

Although we cannot ascertain whether this increase is due to higher use of nephrotoxic anticancer drugs or increase of cancer incidence before 2005, improved cancer survival in France in the most recent period may be a key contributor to cancer-related ESKD increase (3,4). Of note, the sex ratio for nephrotoxin-related ESKD was similar to that reported for the overall French dialysis population (23), whereas it was much higher for urinary tract cancer, as expected from well documented sex disparities in this cancer incidence (24).

Patient characteristics at dialysis initiation were similar to those from other studies, with a lower prevalence of comorbidities among those with cancer-related causes than among other patients with ESKD, and their preference for hemodialysis rather than peritoneal dialysis (13,25). The lower prevalence of comorbidities in these patients may reflect some selection process resulting from the evaluation of overall prognosis and treatment options for each patient and then by shared decision-making about starting dialysis (13).

Our findings about mortality in patients with ESKD related to nephrotoxins or urinary tract cancer are difficult to compare with other studies where malignancy status at dialysis initiation was not available. Like others, we found that these patients had worse survival than patients with other ESKD causes when they were reported to have had active malignancy at dialysis start (11,13). When they did not have an active malignancy, adjusted SHR for all-cause mortality was similar, consistent with the better survival observed for patients with renal cell cancer undergoing nephrectomy (13). Nevertheless, in these patients without active malignancy, cancer mortality remained higher than in controls.

Kidney transplantation is the gold-standard KRT in ESKD, for both survival and quality of life (26). Among the patients who begin hemodialysis, early transplantation improves long-term outcomes (11). In this study, both patients with urinary tract cancer– and nephrotoxin-related ESKD whose cancer was not active at dialysis start had a lower rate of access to the transplant waiting list than their matched controls. However, once on the waiting list, their probability of transplantation was similar to that of their controls. Several factors may partly explain this limited access for patients with cancer-related ESKD. Pelvic radiation for urinary tract, gynecologic, or colorectal cancers can cause tissue injury that leads to radiation-induced atherosclerosis, atrophy, tissue ischemia, and fibrosis (27). Hence, kidney transplantation in these patients may be impossible due to extreme tissue frailty and, consequently, be definitively contraindicated (28). Complex urologic, gynecologic, and gastrointestinal oncologic surgery with local tissue impairment may also prevent

Table 3. Number of events and crude and adjusted subdistribution hazard ratios for mortality on dialysis, wait-listing, and kidney transplantation

Outcome	Nephrotoxin-Related ESKD					Urinary Tract Cancer–Related ESKD				
	Controls	Patients with Active Malignancy	*P* Value	Patients without Active Malignancy	*P* Value	Controls	Patients with Active Malignancy	*P* Value	Patients without Active Malignancy	*P* Value
Mortality on dialysis										
Number of patients	2368	174		113		9380	683		474	
Number of deaths	802	124		47		4335	420		247	
Crude SHR (95% CI)	Reference	3.7 (3.0 to 4.7)	<0.001	1.3 (1.0 to 1.8)	0.05	Reference	1.7 (1.5 to 1.9)	<0.001	1.1 (0.9 to 1.2)	0.7
Adjusted SHR (95% CI)[a]	Reference	4.2 (3.2 to 5.5)	<0.001	1.4 (0.9 to 2.0)	0.3	Reference	2.0 (1.7 to 2.2)	<0.001	1.1 (0.9 to 1.2)	0.9
Wait-listing[b]										
Number of patients	1911	146		88		5113	404		225	
Number of events	919	12		29		1936	45		55	
Crude SHR (95% CI)	Reference	0.20 (0.11 to 0.34)	<0.001	0.67 (0.5 to 0.90)	<0.001	Reference	0.33 (0.25 to 0.45)	<0.001	0.51 (0.40 to 0.67)	<0.001
Adjusted SHR (95% CI)[c]	Reference	0.19 (0.11 to 0.32)	0.03	0.62 (0.43 to 0.88)	0.01	Reference	0.28 (0.21 to 0.37)	<0.001	0.47 (0.36 to 0.60)	<0.001
Kidney transplantation[d]										
Number of patients	919	12		29		1935	45		55	
Number of events	597	8		14		1277	24		32	
Crude SHR (95% CI)	Reference	1.2 (0.44 to 3.1)	0.7	0.67 (0.40 to 1.2)	0.2	Reference	0.91 (0.60 to 1.4)	0.6	1.0 (0.7 to 1.5)	0.9
Adjusted SHR (95% CI)[c]	Reference	1.1 (0.40 to 3.2)	0.6	0.65 (0.40 to 1.4)	0.6	Reference	0.90 (0.60 to 1.2)	0.6	1.0 (0.8 to 1.6)	0.5

SHR, subdistribution hazard ratio.
[a]SHR adjusted for sex, age at dialysis initiation, diabetes status, cardiovascular comorbidities, liver disease, respiratory disease, and emergency dialysis.
[b]Among patients aged <75 yr.
[c]SHR adjusted for sex, age at dialysis initiation, diabetes status, cardiovascular comorbidities, and temporary transplantation contraindication.
[d]Among patients aged <75 yr wait-listed for kidney transplantation.

surgeons from performing transplantation because of the high risk of early graft failures (29).

Kidney transplant candidates with a history of malignancy usually face waiting times even longer than most because of the challenging nature of decision-making related to their high risk of cancer recurrence and mortality (30,31). Clinical practice guidelines on the evaluation and management of candidates for kidney transplantation recommend excluding those with active malignancy and waiting from 2 to 5 years after completion of potentially curative cancer treatment, depending on the cancer type and stage (16,32–34). These waiting times often relied on high recurrence rates based on old retrospective studies (35,36). It is worth noting, however, that a study in Norway—where the transplantation rate is very high—showed that the Norwegian policy of a short 1-year waiting period between cancer treatment and kidney transplantation yielded similar overall survival for kidney transplant recipients with and without a cancer history (37). This difference in clinical practice between France and Norway may lead to more studies to determine whether the wait-listing time should be shortened.

Our study has several strengths including the availability of ESKD causes from the most commonly used nephrotoxins over a 10-year period and the unselected nature of the REIN registry population, which enables our findings to be generalized to all patients on dialysis in France. Most importantly, patients' malignancy status was known at dialysis initiation, whether it was active before then or not. This allowed assessment of both mortality and transplantation access by subgroup according to this critical determinant of both outcomes, involving 60% of all cases.

This study also has limitations. The type and grade of underlying cancer for patients with nephrotoxin-related ESKD was unknown, which prevented us from assessing mortality by malignancy type. Likewise, the type of nephrectomy, whether radical or partial, was not recorded, so we could not estimate the percentage of patients with ESKD after surgery. Similarly, CKD status at cancer onset was unavailable. In some cases, non-neoplastic diseases were also reported at dialysis start, but the low percentage of biopsy-proven diagnoses makes it difficult to determine the relative contribution of each presumed cause in the onset of ESKD. We cannot rule out, however, that it may have been multifactorial in some cases. Finally, the duration of cancer remission for those without reported active malignancy at baseline was not recorded which prevented us from estimating the wait-listing rate in patients in remission for >5 years. The number of kidney transplants was also too low to draw meaningful conclusions about this outcome.

Improvement in cancer survival appears to be associated with an increase in KRT for ESKD related to antineoplastic treatments. Our study indicates that survival among patients starting dialysis with cancer-related ESKD, but whose cancer had not been active in the previous 2 years, is similar to that of other patients with ESKD of similar age, sex, and diabetes status. Nonetheless, and despite their lower prevalence of comorbidities than patients with other ESKD causes, these patients were less likely to be wait-listed for transplantation. Uncertainties regarding the optimal waiting time before transplantation for many cancers and fear of cancer recurrence remain major obstacles to wait-listing patients in remission. Further studies are needed to evaluate the best timing for kidney transplantation in patients with ESKD after cancer treatment. Close collaboration between nephrologists and oncologists is needed to improve decision-making about kidney transplantation in this rapidly growing patient population to further improve their quality of life and outcomes.

Data Sharing

Data are available upon request to the REIN registry by contacting the coordinator Dr. Jacquelinet (email: christian.jacquelinet@biomedecine.fr).

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Disclosures

Dr. Alencar de Pinho, Dr. Béchade, Dr. Devathaire, Dr. Haddy, Dr. Jacquelinet, Dr. Lassalle, Dr. Mansouri, Dr. Snanoudj, Dr. Stengel, and Dr. Vigneau have nothing to disclose.

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Supplemental Material

This article contains the following supplemental material online at http://cjasn.asnjournals.org/lookup/suppl/doi:10.2215/CJN.10230819/-/DCSupplemental.

Supplemental Table 1. Studied causes of ESKD by subtype, coded according to the International Classification of Disease (ICD10).

Supplemental Table 2. Standardized incidence rates of cancer-related ESKD per million inhabitants, overall and by subtype, age, and sex, 2006–2015.

Supplemental Figure. Access to kidney transplantation among wait-listed patients with cancer-related ESKD and matched controls.

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