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Human immunodeficiency virus-related renal cell carcinoma: a 13.5-year experience

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Abstract

Background Few reports have focused on renal cell carcinoma (RCC) in the people with HIV(PWH).

Methods We analyzed patients diagnosed with RCC at our center between January 2011 and June 2024, divided into groups based on their HIV status. Categorical variables were compared using the chi-square test, and continuous variables were analyzed with the t-test. We estimated median and 1-, 3-, and 5-year cancer-specific survival (CSS) using Kaplan–Meier curves and conducted univariate and multivariate Cox analyses to evaluate variables associated with CSS.

Results In total, 144 RCC patients were assigned to either PWH group ($n=48$) or PWoH (people without HIV) group ($n=96$). Patients in the PWH group were significantly more likely to be male (91.7% vs. 71.8%, $p=0.014$), and their median age was 7 years younger than that in the PWoH group (51 vs. 58 years, $p<0.01$). Both groups had small-diameter, early-stage, low-grade tumors, with no significant differences in short-term outcomes. Higher tumor stage (>T1 vs. T1: hazard ratio = 8.621, 95% confidence interval = 3.76–20, $p<0.01$) and larger tumor diameter (≥ 7 vs. <7 cm: hazard ratio = 3.525, 95% confidence interval = 1.697–7.321, $p<0.01$) were significantly associated with CSS, whereas the HIV status did not significantly affect long-term survival.

Conclusions RCC tends to be diagnosed at a younger age in PWH, highlighting the need for earlier RCC screening in this population. The HIV status does not affect postoperative recovery, short-term outcomes, or long-term survival in patients with RCC.

Keywords Human immunodeficiency virus, Renal cell carcinoma, Surgery, Perioperative period, Outcomes, Survival

Introduction

Human immunodeficiency virus (HIV) infects dendritic cells, macrophages, and $CD4^+$ T cells, leading to destruction of the immune system. This not only predisposes individuals to opportunistic infections but also increases their risk of various cancers [1, 2]. In 2012, an International Agency for Research on Cancer working group demonstrated that HIV infection plays a causal role in Kaposi sarcoma, non-Hodgkin lymphoma, Hodgkin lymphoma, and cancers of the cervix, anus, and conjunctiva [3]. With improved survival among people with HIV(PWH), the incidence of certain malignancies,

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including lung and colorectal cancer, has also increased [4, 5].

Renal cell carcinoma (RCC) is a common genitourinary tumor, with 0.388 million new cases and 0.17 million deaths reported worldwide in 2021 [6]. However, there are limited reports on RCC in PWH. To the best of our knowledge, Gardenswartz et al. reported the first case of RCC associated with HIV infection in 1984 [7]. This case involved a 38-year-old African American man with Kaposi sarcoma and cytomegalovirus infection, in whom the authors suggested that RCC onset was associated with HIV infection. Since then, occasional reports of RCC in PWH have emerged from France, the United States, India, and Africa [8–10].

In 2008, a trans-Atlantic case series included nine PWH with RCC. The clinical presentations and features of RCC in these patients appeared similar to those in the HIV-negative population, leading the authors to conclude that HIV had a less significant role in tumor progression than age and exposure to risk factors. They suggested that RCC should be classified as a non-AIDS-defining cancer [11]. In 2016, a study at a state referral center in Australia identified nine patients with RCC who also had HIV infection. Data on presentation, management, and outcomes were collected from these patients' medical records, with findings indicating that treatment options for PWH should align with those for the general population. The study further suggested that favorable outcomes could be achieved through radical surgery despite an immunodeficient status [12].

The most recent study on RCC in PWH, conducted at our center in China, involved 19 cases. We retrospectively analyzed these patients' clinical characteristics, treatments, pathology results, and outcomes. Our findings indicated that the outcomes of partial nephrectomy were comparable to those of radical nephrectomy, supporting partial nephrectomy as a beneficial approach for young PWH with RCC who are concerned about recurrence and metastasis due to immunodeficiency [13].

However, none of the previous studies included a sufficient number of cases or follow-up duration to enable statistically significant conclusions. In this study, we compared the demographics, clinical characteristics, tumor features, perioperative data, pathology, short-term outcomes, and long-term survival between patients with and without HIV infection to improve clinicians' understanding of PWH with RCC.

Methods

This retrospective study involved patients diagnosed with RCC and treated between January 2011 and June 2024 in the Department of Urology at Beijing Youan Hospital, affiliated with Capital Medical University. This hospital also houses the largest HIV follow-up facility in China. RCC Patients were divided into PWH group and PWoH group. To specifically assess the effect of HIV infection on RCC, patients with end-stage organ disease, those on long-term immunosuppressive therapy, and those with other chronic infectious diseases or malignancies were excluded from both groups.

Data on patient demographics, clinical characteristics, tumor features, perioperative information, pathology, and short-term outcomes were extracted from the medical records. We also focused on long-term survival by measuring cancer-specific survival (CSS), calculated from the date of surgery to the date of cancer-related death or the last follow-up. Additionally, we collected data on the HIV status, including the $CD4^+$ T-lymphocyte count, viral load at RCC diagnosis, and duration of antiretroviral therapy (ART).

The study protocol was reviewed and approved by the Ethics Committee of Beijing Youan Hospital, affiliated with Capital Medical University (approval number [2020]035; archive number LL-2019-176-K). Informed consent was obtained from all patients whose data were included in this study.

Categorical variables were analyzed using the chi-square test, and continuous variables were examined with the t-test in the univariate analysis. Kaplan–Meier curves were used to estimate the median and the 1-, 3-, and 5-year CSS rates. Univariate and multivariate Cox regression analyses were conducted to evaluate variables associated with CSS. All statistical analyses were performed using SAS software, version 9.3 (SAS Institute Inc., Cary, NC, USA). A p-value of < 0.05 was considered statistically significant.

Results

Demographics, clinical characteristics, and HIV status

In total, 150 patients were diagnosed with RCC during the study period. After excluding six patients (three with coexisting malignancies, one with hepatitis C, one with liver transplantation, and one with end-stage renal disease), the remaining RCC patients were assigned to either PWH group ($n = 48$) or the PWoH group ($n = 96$). Patient demographics at the time of RCC diagnosis and clinical characteristics, stratified by HIV status, are presented in Table 1.

Both groups exhibited male predominance, with a significantly higher proportion of men in the PWH group (91.7% vs. 70.8%, $p = 0.005$). The median age was significantly lower in the PWH group (51 vs. 58 years, $p < 0.01$). Hypertension was the most common comorbidity and was significantly more prevalent in the PWoH group than in the PWH group (49.0% vs. 20.8%, $p < 0.01$). There was no significant difference between groups in the proportion of patients with a smoking history of > 10 years (25.0% vs. 19.8%).

Table 1 Demographics at the time of RCC diagnosis and clinical characteristics of the patients

Variables	PWH ($n=48$)	PWoH ($n=96$)	*P* value
Median age(range)	51(30–73)	58(32–83)	< 0.01
Male, n(%)	44(91.7%)	68(70.8%)	0.005
MSM, n(%)	20(41.7%)	0	< 0.01
Comorbidities, n(%)			
Hypertension	10(20.8%)	47(49%)	< 0.01
Diabetes	7(14.6%)	18(18.75%)	0.534
CKD	0	1	0.095
CAD	0	8(8.3%)	
CVD	0	0	
Smoking, n(%)	12(25.0%)	19(19.8%)	0.473
Presentation, n(%)			
Incidental	40(83.3%)	79(82.3%)	0.876
Triad	0	1	
Flank pain	4	14	
Hematuria	4	2	
Palpable mass	0	0	
ART duration, n(%)	13(27.08%)		
< 2 years	15(31.25%)		
>2 years	20(41.67%)		
No HAART			
HIV RNA, n(%)	13(27.1%)		
TND	8(16.7%)		
<500 copies/ml	15(31.25%)		
>500 copies/ml	12(25.0%)		
NT			
$CD4^+$ T cells, n(%)	427 cells/ul		
Median	10(20.8%)		
<200 cells/ul	38(79.2%)		
>200 cells/ul			

Abbreviations: CAD = coronary artery disease; CKD = chronic kidney disease; CVD = cerebrovascular disease; ART = antiretroviral therapy; HIV = human immunodeficiency virus; MSM = men who have sex with men; NT = not tested; TND = target not detected

The most common clinical presentation of RCC in both groups was incidental findings on imaging (83.3% in the PWH group and 82.3% in the PWoH group), followed by flank pain and hematuria. Only one patient (PWH group) presented with the classic triad of hematuria, flank pain, and a palpable mass.

In the PWH group, 20 patients were diagnosed with RCC and HIV infection simultaneously, while 28 patients had been receiving ART for a median of 36 months (range, 4–108 months) prior to RCC diagnosis. The viral load was measured before surgery in 36 PWH, with levels classified as "target not detected" or < 500 copies/mL in 21 cases. The median $CD4^+$ T-lymphocyte count at RCC diagnosis was 427 cells/μL (range, 111–1536 cells/μL).

Tumor characteristics and pathology

The tumor characteristics and pathological data are summarized in Table 2. The median tumor diameter was slightly, but not significantly, smaller in the PWH group than in the PWoH group (4.53 vs. 4.65 cm). Most of the RCC tumors in both groups were classified as stage T1 (66.7% in the PWH group vs. 62.5% in the PWoH group, $p > 0.05$). Clear cell carcinoma was the most common pathological type in both groups, with a few rare pathological types observed in each group. There was no significant difference in the Fuhrman tumor grade between the groups; most tumors were grade 1 or grade 2 (75.0% in the HIV-positive group vs. 83.3% in the HIV-negative group, $p > 0.05$).

Perioperative data and short-term outcomes

Perioperative data and short-term outcomes are summarized in Table 3. All patients underwent surgery. In the PWH group, the procedures comprised partial nephrectomy ($n=8$), laparoscopic radical nephrectomy ($n=39$), and removal of a tumor thrombus from the inferior vena cava ($n=1$). In the PWH group, the procedures comprised laparoscopic partial nephrectomy ($n=16$), laparoscopic radical nephrectomy ($n=70$), open radical nephrectomy ($n=9$), and removal of a tumor thrombus from the inferior vena cava ($n=1$).

There was no significant difference between groups in the proportion of patients who underwent radical nephrectomy, and no patients required conversion from laparoscopic to open surgery in either group. The operation time was slightly longer in the PWH group than in the PWoH group (4.21 vs. 3.88 h), although the difference was not statistically significant. Estimated blood loss was

Table 2 Tumor characteristics and pathologic data

Variables	PWH (*n* = 48)	PWoH (*n* = 96)	*P* value
Laterality, n(%)	24(50%)	32(33.3%)	0.053
Right kidney	24(50%)	64(66.7%)	
Left kidney			
Tumor diameter(cm)	4.53 ± 2.28	4.65 ± 2.56	0.773
Tumor stage, n(%)	32(66.7%)	60(62.5%)	0.624
T1	16(33.3%)	36(37.5%)	
> T1			
Pathological type, n(%)	44(91.7%)	80(83.3%)	0.173
ccRCC	4(8.3%)	16(16.7%)	0.317
nccRCC	3(6.2%)	5(5.2%)	
Papillary	1(2.1%)	2(2.1%)	
Chromophobe	0(0%)	9(9.4%)	
Sarcoma	36(75%)	80(83.3%)	
Tumor grade(n,%)	12(25%)	16(16.7%)	
Grade1-2	0	0	
Grade 3–4			
Positive margines			

Abbreviations: ccRCC = clear cell renal cell carcinoma; nccRCC = non-clear cell renal cell carcinoma

Table 3 Perioperative data and short-term outcomes in all cases

Variables	PWH (*n* = 48)	PWoH (*n* = 96)	*P* value
Operative methods, n(%)	8(16.7%)	16(16.7%)	1
LPN	40(83.3%)	80(83.3%)	0.127
RN	0	0	
Open conversions	4.21 ± 0.93	3.88 ± 1.64	
Operative time(h)			
Blood loss(ml)	95 ± 164	233 ± 334	0.037
>500 ml	4(8.3%)	17(17.7%)	
<500 ml	44(91.7%)	79((82.3%)	
TRDT(d)	6.78 ± 1.89	7.62 ± 3.65	0.077
Hospital stay(d)	16.54 ± 3.87	19.02 ± 8.61	0.019
Compications, n(%)	7(14.6%)	24(25%)	0.152
Transfusion	1	5	
Fever	1	6	
Ileus	0	0	
Wound	4	10	
Pneumonia	1	2	
Stenocardia	0	1	
DVT	0	0	
UTI	0	0	
Inhospital mortality	0	0	
30-day mortality	0	0	

Abbreviations: DVT = deep vein thrombosis; LPN = laparoscopic partial nephrectomy; RN = radical nephrectomy; TRDT = time to removal of drainage tube; UTI = urinary tract infection

significantly lower in the PWH group than in the PWoH group (95 vs. 233 mL, $p < 0.01$).

No significant differences were observed between the groups in terms of the time to drainage tube removal, length of hospital stay, or postoperative complications. However, the hospital stay was significantly longer in the PWH group than in the PWoH group (19.02 vs. 16.54 days, $p = 0.019$). The most common postoperative complications were wound-related. No in-hospital or 30-day mortality occurred in either group.

Long-term survival

The mean follow-up duration was 85 months. Kaplan–Meier analysis (Table 4; Fig. 1) showed that the 1-, 3-, and 5-year CSS rates were 95.8%, 93.3%, and 80.2% in the PWH group compared with 93.8%, 87.4%, and 82.9% in the PWoH group, respectively. The median CSS was 114 months for the entire cohort, 100 months for the PWH group, and 122 months for the PWoH group; however, these differences were not statistically significant ($p = 0.253$).

Univariate analysis of HIV status, sex, age, tumor stage, tumor grade, tumor diameter, histologic subtypes, and

Table 4 Cancer-specific survival in the two study groups

Survival	PWH Group	PWoH Group
1 year	95.8%	93.8%
3 year	93.3%	87.4%
5 year	80.2%	82.9%
Median Survial (mo)	100	122

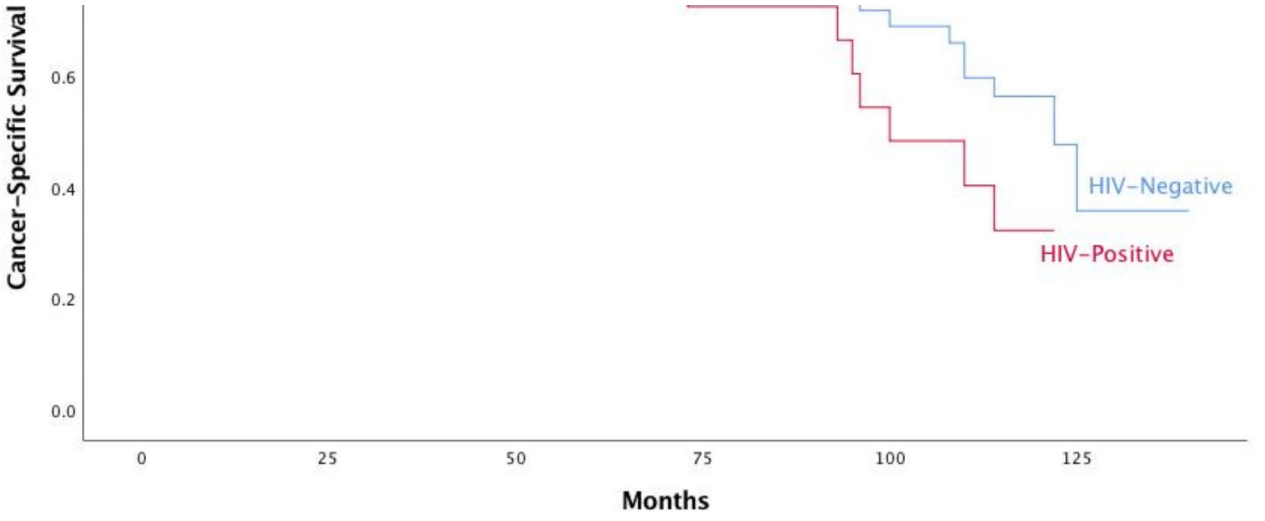

Fig. 1 Kaplan–Meier cancer-specific survival curve of patients with RCC by HIV status

surgical procedure showed that a larger tumor diameter and higher tumor stage were significantly associated with CSS. In the multivariable analysis (Table 5), a higher tumor stage (Stage > T1 vs. T1: hazard ratio = 8.621, 95% confidence interval = 3.76–20, $p < 0.01$) and larger tumor diameter (≥ 7 vs. <7 cm: hazard ratio = 3.525, 95% confidence interval = 1.697–7.321, $p < 0.01$) remained significantly and independently associated with CSS. The HIV status, tumor grade, age, sex distribution, histologic subtypes, and surgical procedure did not have a significant effect on long-term survival. Considering the significant effect of higher tumor stage on CSS, we performed Kaplan–Meier analysis among the patients with higher tumor stage(Stage > T1) by HIV status(Fig. 2), and the results showed no statistically significant difference($p = 0.230$). When the analysis was restricted to the 48 HIV-infected cases and evaluated for the effect of ART duration before diagnosis of RCC, HIV viral load at the time of RCC diagnosis, and nadir $CD4^+$ lymphocyte count, no variables found to be independently associated with survival.

Discussion

The significant reduction in HIV-related mortality since the introduction of ART is well documented, and HIV infection is increasingly regarded as a chronic disease rather than an acute, life-threatening illness [14]. At our center, which includes the largest HIV follow-up service in China, an increasing number of patients diagnosed with urogenital tumors are HIV-positive. In this study, we analyzed 13.5 years of accumulated data on patients with RCC, the most common type of urogenital cancer seen at our center, according to HIV status.

We found that the age at RCC diagnosis in PWH (51 years) was notably younger than in our control group and the general population (60 years) but was comparable to the Australian PWH (52 years) [15, 16]. This finding underscores the importance of initiating RCC screening earlier in PWH.

Regarding the sex distribution, RCC is generally more common in men than in women, with a 2:1 ratio of new diagnoses in the general population [16]. In our study, this male predominance was even more pronounced, with 91.7% of PWH with RCC being male. This reflects the substantial proportion (41.7%) of men who have sex with men in our cohort and aligns with the increasing prevalence of AIDS among men who have sex with men in China [17].

A trans-Atlantic case series involving nine RCC patients with HIV infection revealed that seven had a history of smoking, suggesting smoking as a risk factor for RCC in this population [10]. However, although smoking, obesity, hypertension, and chronic kidney disease are known risk factors for RCC in the general population [18], our study's small sample size and the relatively low

Table 5 Multivariable Cox proportional hazards model for cancer-specific mortality in patients with RCC

Variable	HR (95% CI)	*P* value
Age	1.022(0.990–1.056)	0.17
Gender	Reference	0.255
Female	1.606 (0.710–3.633)	
Male		
Surgical procedure	Reference	
PN	1.024(0.337–3.115)	
RN		
Tumor diameter	Reference	< 0.01
< 7 cm	3.525(1.697–7.321)	
≥ 7 cm		
Histologic subtypes	Reference	0.649
ccRCC	1.197(0.552–2.595)	
nccRCC		
Tumor grade	Reference	0.412
Grade1-2	1.114(0.866–1.441)	
Grade3-4		
Tumor stage	Reference	< 0.01
T1	8.621(3.76-20)	
> T1		
HIV status	Reference	0.594
HIV-negative	1.227(0.578–2.608)	
HIV-positive		
CD4 + T cells (cells/ul)	Reference	0.493
< 200 cells/ul	0.588(0.129–2.684)	
> 200 cells/ul		
HIV virus load(copies/ml)	Reference	0.659
< 1000	1.493(0.252–8.830)	
>1000		
HIV duration	Reference	0.844
<1 month	1.228(0.159–9.483)	
>1 month		

Abbreviations: CI = confidence interval; HR = hazard ratio; PN = partial nephrectomy; RN = radical nephrectomy

proportion of patients with a long-term smoking history limit our ability to draw conclusions in this regard.

Most of our patients presented with incidental findings on an imaging examination regardless of HIV status. Only one patient presented with the classic triad of symptoms, which is consistent with previous reports and can be attributed to advances in screening methods [19].

We assessed the patients' immune status by measuring the $CD4^+$ T-lymphocyte count and HIV load, and we found that over half of the PWH had been on ART for a median of 36 months before RCC diagnosis and had relatively stable immune function. Regular long-term ART may contribute to favorable short-term outcomes with fewer perioperative complications in PWH with RCC.

The influence of the $CD4^+$ count and HIV load on surgical outcomes has been previously investigated. Early studies indicated that a lower viral load was associated with fewer postoperative complications in PWH undergoing various surgeries [20]. More recent research on PWH with colorectal cancer showed postoperative outcomes comparable to those in the general population [21]. Lower $CD4^+$ counts, particularly < 200 cells/μL, have been linked to a higher likelihood of emergency surgery and increased morbidity and mortality [22, 23]. However, in the present study, we did not stratify the viral load or $CD4^+$ count because of the low incidence of postoperative complications.

In the general population, approximately 60–85% of patients with RCC present with stage T1 disease [24]. The frequency of T1 disease in our study was within this range regardless of HIV status, which may predict better outcomes. The 2004 World Health Organization classification of adult renal tumors categorizes RCC into several histological subtypes, including clear cell, papillary, and chromophobe, which account for approximately 70%, 10–15%, and 5% of RCC cases, respectively [25]. In our series, clear cell carcinoma was the most common subtype in PWH and PWoH(91.7% and 83.3%, respectively).

The Fuhrman grade is widely recognized as a key histological indicator of the prognosis. A large United States study involving 5453 patients with RCC showed that most patients had Fuhrman grade 2 disease and favorable outcomes [26]. In our study, most patients also had relatively low tumor grades, irrespective of their HIV status. This finding is somewhat unexpected because immunodeficiency due to HIV is commonly associated with

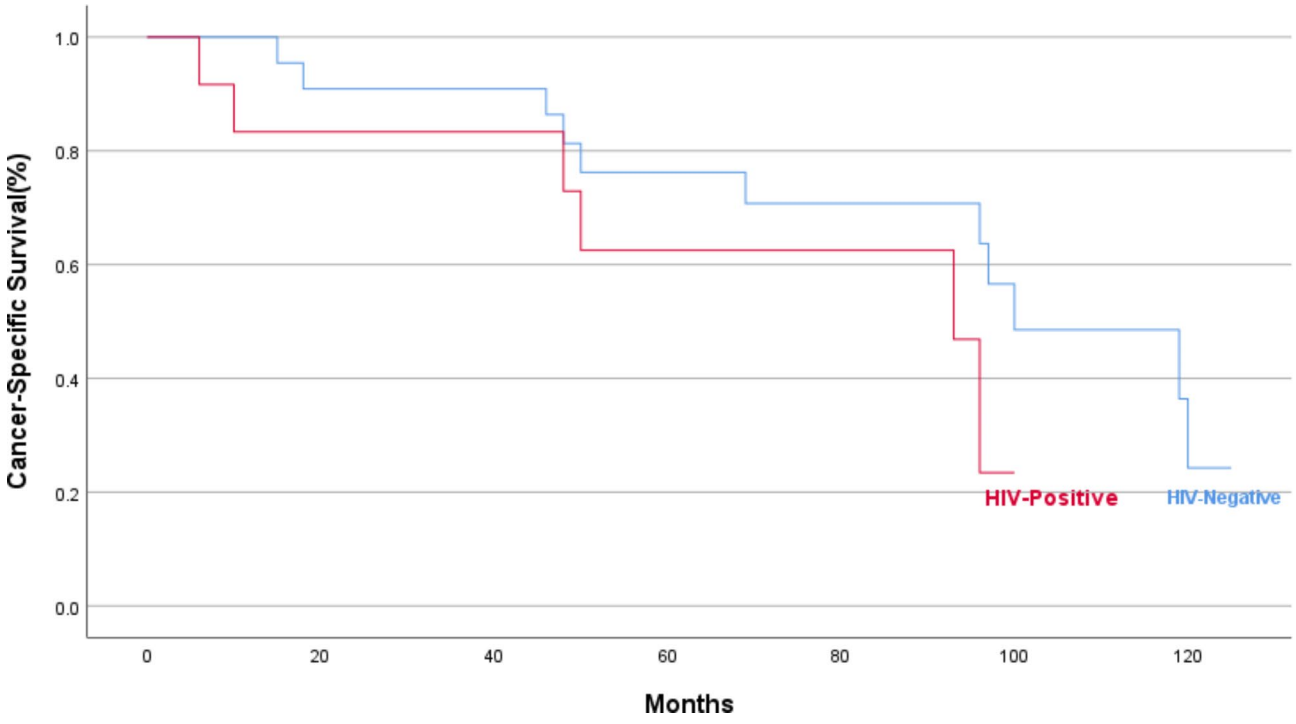

Fig. 2 Kaplan–Meier cancer-specific survival curve of patients with higer tumor stage by HIV status

a higher tumor stage and grade. However, it may reflect advancements in antiviral therapy and the widespread use of ART.

Partial nephrectomy is recommended for patients with T1 tumors to achieve complete resection of the primary tumor while preserving as much healthy renal parenchyma as possible. Compared with radical nephrectomy, partial nephrectomy is associated with less renal function impairment and comparable oncological outcomes, although its impact on overall survival remains debated [27]. Surgical guidelines for RCC treatment in PWH mirror those for the general population, and we did not exclude partial nephrectomy in PWH because of concerns about immunodeficiency-related recurrence. Instead, surgical feasibility was the primary factor guiding decision-making, regardless of HIV status, and partial nephrectomy did not result in residual disease or recurrence in PWH. Additionally, partial nephrectomy is being increasingly performed in younger patients. Available evidence, including findings from our study, indicates that RCC tends to be diagnosed at a younger age in PWH, who may benefit from partial nephrectomy if they are receiving regular ART.

We found no significant differences between the two study groups in time to drainage tube removal, length of hospital stay, or postoperative complications, suggesting that HIV infection does not delay postoperative recovery. Moreover, there were no life-threatening (Clavien–Dindo grade IV) postoperative complications in either group, challenging the common assumption that PWH have an elevated risk of severe infectious complications following surgery.

Previous studies have revealed varying findings regarding the most common postoperative complications. For instance, a South Korean study of 127 patients with RCC identified blood transfusion and atelectasis as the most frequent postoperative complications [28]. Conversely, a United States study involving 102 patients with RCC showed that ileus was the most common postoperative complication, occurring in up to 6% of cases regardless of surgical approach [29]. Other literature indicates that complications are generally infrequent and predominantly minor [30–33]. In our series, blood loss was greater in the PWH group, likely because of the higher proportion of sarcomas in this group. Sarcoma is associated with larger tumor size, a richer blood supply, and increased peripheral blood vessel invasion [34], which may contribute to a higher likelihood of blood loss exceeding 500 mL during surgery.

Both groups had favorable short-term outcomes, with no in-hospital or 30-day mortality. This may be attributed to the minor postoperative complications and effective antiviral therapy in PWH. In terms of long-term survival, patients with RCC who underwent surgery demonstrated strong 5-year CSS rates and median CSS, regardless of their HIV status (80.2% vs. 82.9%; 100 vs. 122 months), consistent with previous studies on postoperative survival in RCC [35–37].

Our analysis showed that higher tumor stage and larger tumor diameter were independently associated with worse CSS. This finding aligns partially with prior studies, which identified higher tumor stage, tumor grade, and larger tumor volume as factors associated with poorer survival.[35,36] These results suggest that HIV status does not impact long-term RCC survival, but rather that tumor aggressiveness plays a critical role. Even when PWH were stratified according to CD4 level, ART duration, and HIV viral load, there were still no variables that could influence survival prognosis. This conclusion was inconsistant with the findings from studies on HIV-related lung cancer, which found that nadir $CD4^+$ lymphocyte cell count less than 200 was associated with worse survival.[5] The results suggested that RCC was more pronounced to be a non-AIDS-defining cancer compared to lung cancer.

This study is limited by its relatively small sample size, which is unavoidable given the rarity of PWH with RCC. Our findings should be considered preliminary and await confirmation in future studies. With a larger cohort, we hope to conduct more systematic research in this patient population. Additional limitations include the single-institution setting and the retrospective nature of the study.

Conclusions

The clinical characteristics, tumor features, perioperative data, pathology, and outcomes in PWH with RCC are comparable to those of PWoH. RCC is typically diagnosed at a younger age in PWH, underscoring the need for earlier screening in this population. Partial nephrectomy should be considered as a surgical option for younger PWH who are on regular ART. Our findings on postoperative complications, hospital stay duration, drainage tube removal time, and short-term outcomes suggest that HIV infection does not impact postoperative recovery or the safety of surgery in patients with RCC. Additionally, HIV infection does not appear to affect the 1-, 3-, or 5-year CSS of RCC based on our institution's data.

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Author contributions
MZ and ZZ contributed research design, data collection, and manuscript writing/editing. XH, and YZ revised the manuscript. All authors reviewed the manuscript.

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Data availability
No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate
The research was reviewed and approved by the Ethics Committee of Beijing Youan Hospital Capital Medical University. The Ethics Committee archive number is LL-2019-176-K, and the approval number is [2020]035. Patients themselves and their family members provided informed consent.

Consent for publication
Written informed consent for publication was obtained from all participants. A copy of the written consent is available for review by the editor of this journal.

Competing interests
The authors declare no competing interests.

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