Invited Review Article

# Urological malignancies in kidney transplant recipient patients

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## Abstract

Kidney transplantation is now established as the ideal treatment option for end-stage renal disease (ESRD) and renal cell carcinoma (RCC) patients. Since the first kidney transplant in the 1970s, research has allowed us to understand the long term sequelae of kidney transplant patients (TXPs) including the risks of increased malignancy from immunosuppression.

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## Introduction

Renal transplantation started in the 1970s.[1,2] In the initial days, only 20 deceased donor kidney transplants were performed between 1970 and 1976. In comparison, data from 2021 Singapore's Renal Registry reflected 555 kidney transplants performed from 2016 to 2021.[3] The advances made to immunosuppressive therapy, legal regulations implemented to improve kidney donation rates, as well as the development of minimally invasive surgical techniques for donor nephrectomy,[4] helped to build the success of kidney transplantation. Compared to kidney dialysis, kidney transplantation is associated with better clinical outcomes in terms of better quality of life and mortality rates, even in the long term.[5] It is the current gold standard of treatment for end-stage renal disease (ESRD). Compared with remaining waitlisted in dialysis, kidney transplantation is associated with improved survival, quality of life for the patients and entails a lower cost for the society.[6]

While kidney transplantation remains the mainstay of treatment for ESRD and RCC patients, the downside of having a kidney transplant is an increased malignancy risk post-transplant. Cancer is one of the leading causes of mortality and morbidity in kidney transplant recipients (TXPs), accounting for 56% of deaths in recipients with a functioning renal graft.[7] A 2017 study done by The American Society of Transplantation and the American Society of Transplant Surgeons revealed that TXPs have a 7-fold risk of renal cell carcinoma (RCC) and 3-fold risk of urothelial carcinoma (UC) compared to the general population.[5] This has been postulated to result from the use of immunosuppressive agents post-transplant, which can cause DNA damage, as well as viral-induced cancers like PTLD (EBV), Kaposi Sarcoma (HHV 8), and HCC (Chronic Hep B, Hep C Viruses) due to the suppression of T-cell functions.

In view of the increased awareness of the importance of malignancies after kidney transplantation, this urological focused article aims to

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discuss the most common and important urological malignancies post-transplant: RCC and UC.

## Renal Cell Carcinoma

### Introduction

RCC accounts for most malignant urological cancers, with a number of subtypes – clear cell (most common), papillary, chromophobe, and medullary. Over the past years, with the increased use of cross-sectional imaging including computed tomography (CT), the detection rates of RCC have increased in both the general population and kidney transplant population. This has led to an improved understanding of the epidemiology, presentation and management of these cancers post transplantation.

### Epidemiology

The risk of RCC in kidney transplant patients is reported to be about 5-10 times higher compared to the general population. It is predominantly (90%) encountered in the native kidneys; and rarely in the kidney allograft.[8] Table 1 summarizes the epidemiological data review of RCC in kidney transplant patients compared with ESRD and the general population.[9] Compared to the general population, it reports the increased lifetime risk of RCC in both ESRD (x3) and kidney TXPs (x5-7), as well as that of the standardised incidence ratio (SIR). Malignancy risk is usually expressed as the SIR, which compares the respective incidence of a malignancy with the rate found in the general population.[10] RCC SIR is approximately 2.6/100,000 in the general population; in comparison to an increased mean rate of 4.87/100,000 in that of ESRD patients, and further increased rate of 9.7/100,000 in kidney TXPs.[9]

Furthermore, in terms of recurrence risk, it has been studied that the risk of RCC recurrence was similar between transplant and dialysis.[11] This is further supported by data from the Frankfurt Transplant Center, where a large number of kidney recipients featured renal cell and urothelial carcinoma among the highest of urological cancers. In this group, 44% actually succumbed to their disease.[12]

Clear cell remains the most common histological RCC subtype, however ESRD patients and TXPs reports increased risks of papillary subtype RCC with incidence of papillary RCC after renal transplantation of up to 30%.[13]

### Risk Factors

Risk factors for RCC specific to each population are listed above (Table 1). Postulated risk factors for the increase in malignancy in a transplanted population are immunosuppression-mediated DNA damage, activation of proto-oncogenes and overexpression of growth factors, interference with DNA repair mechanisms and the loss of immune surveillance and activation of viruses.[9]

**Table 1.** Epidemiological data review of renal cell carcinoma in kidney transplant patients compared with end-stage renal disease and the general population.

| | General population | End-stage renal disease | Kidney transplantation |
|---|---|---|---|
| Lifetime risk | 1.62 % | 3X | 5-7X |
| Standardised incidence rate (/100,000) | 2.6-9.2 | 4.87 (95% CI 4.1-5.7)<br>Younger population | 9.7 (95% CI 5.7-16.5)<br>Biphasic peaks 1st, 4-15 (6) years<br>even younger age |
| Risk factors | Male, age, smoking | + Acquired cystic disease tuberous sclerosis<br>+ Dialysis duration (3 years) | +Lifelong immunosuppression<br>+Retransplants<br>+Viral infections |
| Histology / location | Clear cell 75%<br>Papillary 12 % | Clear cell<br>Papillary 35-45% | Native kidneys > 90%<br>Allograft < 10% |
| Prognosis | T1-T2 - 90% 5-year<br>Advanced - 20% -60%<br>Recurrence -10-30%<br>Metastasis - 13 months survival | Lower stage and grade<br>Acquired cystic disease associated RCC – WHO 2016 classified indolent | 73% early stage<br>Worse survival for late stage |

**RCC in Native Kidneys**

Despite the increased risk of RCC development in TXPs, it has been reported that most RCCs in TXPs happen to be incidental, low-stage, low-grade tumours with good prognosis.[14] These tumours are generally small and asymptotic and their diagnosis is usually incidental.[15] If the cancers are diagnosed pre-transplant, patients with ESRD should still be eligible to be placed on the transplant waitlist with minimal delay after treatment and confirmation of localised low-grade cancers.

Laparoscopic radical nephrectomy is currently the main approach to RCC in native kidneys, and can be done via both the Laparoendoscopic Single Site (LESS) or Retroperitoneoscopic 3 scope approach. Locally, the Retroperitoneoscopic 3 port approach is preferred because it does not involve the transperitoneal space. The retroperitoneal approach is a safe and effective technique which allows for the preservation of peritoneal integrity for pretransplant peritoneal dialysis. Further advantages include ease of kidney access by developing the existing potential retroperitoneal space and avoidance of the transperitoneal approach with the resultant reduced risk of injury to and interference from intra-abdominal organs.[16]

Pre-transplant screening for cancer in the native kidney is controversial. However, it has been advocated as RCC has been reported to be bilateral in 20% of ESRD patients.[17] Current pre-transplant screening recommendations for transplant candidates were typically not well validated. According to the European Renal Best Practice Transplantation Guidelines[18], screening in ESRD patients is usually performed following the same protocols suggested for the general population. This topic currently depends on the opinions of expert clinicians, oncologists and screening specialists. The reasons for screening for early cancers in pre transplant ESRD patients are firstly, if RCC, at discovery of presentation, is of a large size or symptomatically picked up, a 25-30% recurrence rate and subsequent 80% mortality was noted. Secondly, according to the European Association of Urology (EAU)[19] and European Renal Best Practice (ERBP) guidelines, such patients, with more locally advanced cancers, would need to wait for an interval of 2-5 years before being able to be listed for transplant, compared to an immediate waitlist admission for small, low-grade RCC cases as mentioned previously.

National country-wide data has been collected in terms of 3 studies from 2 main transplant centers in Singapore – National University Hospital (NUH) and Singapore General Hospital (SGH). A study was done regarding native kidney RCC, stating the outcomes of TXPs who subsequently developed RCC (Table 2). The first study in NUH involving TXP patients with RCC and ESRD from 2010-2013 showed 10 incidental cases of RCC with 3 symptomatic discoveries. Although outcomes were good for the majority and a 100% survival rate was reported, 2 patients at 3 years progressed to distant metastases – likely those with a higher stage of RCC at diagnosis.[20]

The second study from SGH published in the AJT journal, depicted 10 cases of RCC, all patients of whom initially had native renal cysts.[9] Due to regular follow-up and early detection of the cancers, outcomes and survival were both stellar.

Lastly, the third study, also based in SGH, mainly of ESRD patients, depicted only half of the RCC cases with an incidental discovery. This led to poorer outcomes in terms of staging at the time of surgery, as well as survival rates (90%).[21]

Hence, in accordance with the data in Table 2, NUH Singapore recommends RCC screening of the native kidneys beginning 1 month post-transplant. For patients with native renal cysts, the surveillance interval would be 2 years; for those without, 5 years.

This differs from the EAU 2018 Guidelines, whereby ultrasound was performed annually for advanced chronic kidney disease (ACKD), previous RCC, as well as Von Hippel-Lindau (VHL) patients.[19] However, the cost effectiveness and overtreatment impact of such screening measures is still unknown.

**RCC in Allograft Kidneys**

Found to be much rarer and only occurring in 10% of TXPs with RCC, the prevalence rate of allograft kidney RCC is only 0.2-0.5% amongst all kidney transplant patients.[22] Most occur de-novo, and Singapore locally reports no occult malignancy donor transmission when last studied at the ministry level.

Management of such cancers requires an individualised approach for each patient. Options include nephron sparing approaches including

**Table 2.** Outcomes of kidney transplant patients with subsequent development of native kidney renal cell carcinoma.

| Studies | NUH (2010-2013) Lu J, et al. BJU Int 2014;113:1-37. | SGH (1995-2007) Goh A, et al. Am J Transplant 2011;11:86-92. | SGH (2000-2010) Chen K, et al. Scand J of Urol 2015;49:200-4. |
|---|---|---|---|
| N | 13 (7 Transplantations) | 10 (Transplantations) | 73 (End-stage renal disease) |
| Incidence | 10 | 10 (All native renal cysts) | 41 (56%) |
| Mean age | 54.7±13.7 | 52 (36-65) | 53.6±11.8 |
| Mean years post transplantation | - | 4.6 | - |
| Surgery | 4 Transperitoneum/7 Retroperitoneum/2 Open | 6 Minimally invasive surgery/ 4 Open | 73% Minimally invasive surgery |
| Clavien Dindo classification >2 | 0 | - | - |
| Tumour size | 2.6±2.2 | 2.5 (1.6-5.5) | - |
| Clear cell carcinoma | 6/13 (46%) | 6/10 | 45 (61%) |
| Cancer grade <3 | 6/13 (46%) | - | - |
| Stage 1 | 11 (84.6%) | 9 (90%) | 64 (87.6%) |
| 3 Year follow up | 100% Survival 2 Distant metastasis | 100% Survival 5 Year overall survival 100% | 90% Survival 5 Year overall survival 68.5% |

partial graft nephrectomy, percutaneous radiofrequency ablation or cryoablation vs. radical graft nephrectomy.[23] In all patients, an attempt to preserve kidneys is warranted with nephro-sparing approaches, with the choice of the surgery being done either open or with minimally invasive surgical techniques.

The gold standard would be akin to that of a non-transplanted kidney – a partial nephrectomy for localised RCCs where technically feasible.[24] Specific to allograft kidney RCCs in TXPs, the most commonly attempted approach is open allograft partial nephrectomy, both extra-capsular and extraperitoneal via the previous incision. Careful pre-operative planning is required with the aid of CT scans and other forms of imaging to maintain hilar control. Certain surgical techniques include that of clamping the iliac artery above and below the anastomosis during warm ischemia with the venous outflow unclamped or mass clamping the hilum for dissection. The common goal is to minimise warm ischemic time, or perhaps even establish zero ischemia. This is because clinical evidence has demonstrated that transplanted kidneys with prolonged ischemic time are more susceptible to long-term deterioration.[25]

Figure 1 shows a 46 year old male patient presenting in 2017 with an incidentally 4 cm renal mass in the kidney transplant. A partial nephrectomy was done successfully (Figure 2) with careful planning, and final histology showing high grade pT3a, ISUP G3 RCC resulting from sinus, renal and segmental vein involvement and clear resection margins. In February 2021, almost 4 years post-surgery, the patient was reported to be recurrence free with a functioning graft.

This approach has been reported by a mini-review published in the American Journal of Transplantation done in 2017, analysing 56 studies covering 163 patients and 174 masses. Of these patients, about 131 out of 174 masses were treated with nephron-sparing methods like partial nephrectomies or ablation. In terms of recurrence rates post-partial nephrectomy, the study reported a low rate of 3.6%[23], rather comparable to non-transplanted native kidneys which had partial nephrectomies done.

**Implication on Medical Management**

Post-transplant, to reduce the risk of RCC development, immunosuppression dose reduction and the use of Mammalian target of rapamycin (mTOR) inhibitors (Sirolimus/Everolimus) can

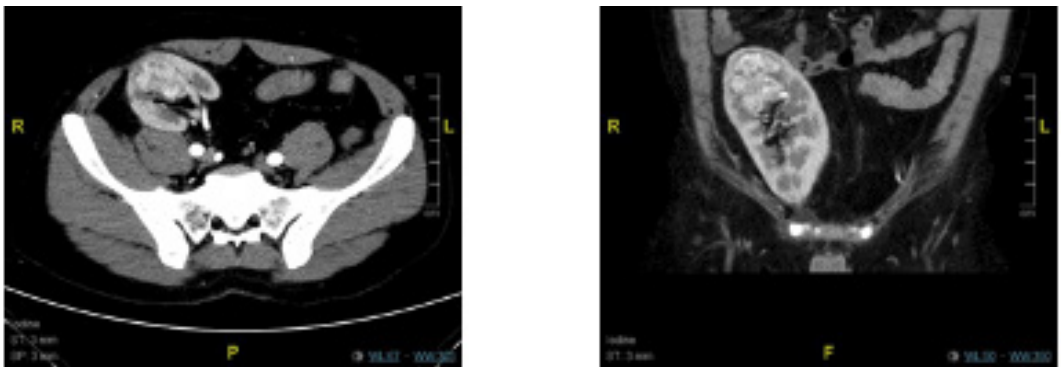


**Figure 1.** 46-year-old male with high grade pT3a, ISUP G3 RCC resulting from sinus, renal and segmental vein involvement and clear resection margins.

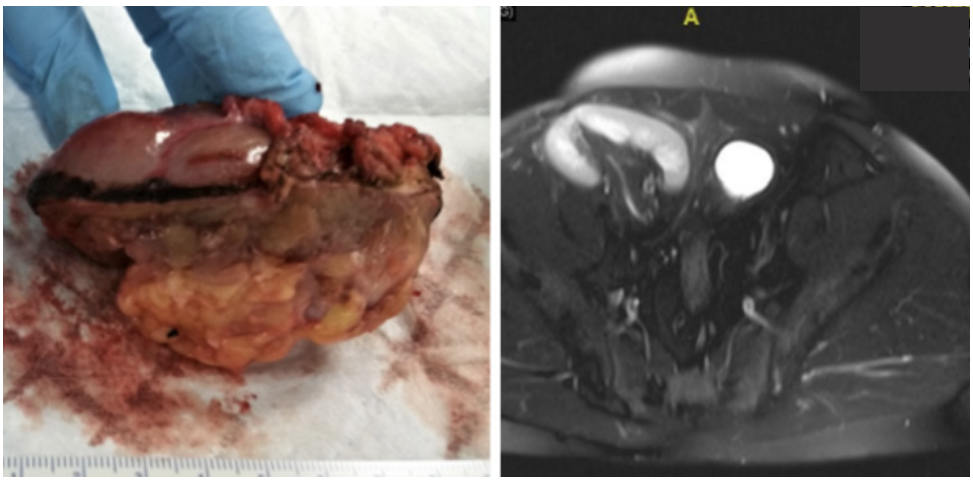


**Figure 2.** Excision of 4 cm renal mass (left); CT scan of the same patient at 4 year work follow-up, depicting a functional graft (right).

be considered.[26] mTOR inhibitors are advocated instead of other anti-proliferatives including mycophenolic acid due to the following reported advantages: less incidence of viral infections (especially, Cytomegalovirus and BK / Human Polyomavirus 1), less neutropenia and low blood platelets, and a possible reduction in long-term incidence of solid neoplasia. Moreover, in low immunological risk patients, mTORi is advocated by some to allow safe minimization of calcineurin inhibitors (CNI), which in the long term could theoretically prolong graft survival.[27]

In the case of metastatic disease, research currently has no consensus for the use of TKI or immune checkpoint inhibitors (ICI). Several studies have revealed that ICI can produce several immune-mediated toxicities involving different organs, such as the skin, the gastrointestinal tract, the liver, and, of course, the kidney. The most frequent lesion of immunotoxicity in the kidney is acute interstitial nephritis (AIN), although other nephropathies have also been described as a consequence of the use of ICI, such as glomerulonephritis and acute thrombotic microangiopathy, among others.[28] Further research is awaited for the use of these agents in TXPs.

## Urothelial Carcinoma

### Epidemiology

UC accounts for about 0.02% incidence rate in the general population. Currently, data on risk recurrence of urothelial carcinoma is scarce.[12] UC incidence among kidney TXPs compared to the general population ranges from 1.6 to 3.3.[29,30] This incidence rate is increased by 3.15x in ESRD patients, and apparently even more in our local Asian population by a further 14x.[31,32] At initial staging, Asian populations were found to have the worst tumour characteristics (muscle invasion, higher grade) at presentation.[33,34] Most TXP patients with urothelial cancers present with bladder cancer (92%), while upper tract urothelial

cancer (UTUC) accounts for the remaining 8%. Median time of presentation from TXP was reported to be 4.5 years from time of transplantation. At presentation, kidney TXPs present with worse tumour characteristics (37% with muscle invasive bladder cancer and 34% with late stage cancer).[35]

The risk factors of UC are well known and include male gender, age, smoking, and use of aristolochic acid.[36] In TXPs, lifelong immunosuppression increases the risk of BKV infection; that has been implicated in the development of urothelial cancer. Evidence from a multivariate study reports an increased risk of 11.6 times of developing UC in TXP patients with BKV infection when compared to general population.[37] There were also higher rates of BK viremia in transplant patients with UC, with a systematic review finding viruria in 29% and viremia in 11% of renal TXPs.[38] The pathophysiology of this is explained by BKV nephropathy resulting in graft dysfunction in transplant patients through several oncogenic mechanisms.[39] This is still under study but a recent 2023 article in American Journal of Transplant suggests certain patterns of BK viral integration that actively contribute to the progression of BKV-associated diseases and thus could be a potential target for disease monitoring and intervention.[40]

Compared to RCC, UC has a significantly poorer prognosis in TXP patients. Currently, the 5 year cancer specific survival is 50%, and the 10 year cancer specific survival has been reported to be as low as 0%.

**Management**

Due to the lower incidence rates of UC, data on their management options are limited. Treatment options including surgery for the management of UC in kidney transplantation are in line with those of non transplant patients.[41,42] With muscle-invasive bladder cancers, the treatment of choice would be radical cystectomy with urinary diversion to the kidney transplant ureter. Neoadjuvant chemotherapy should be equally considered. In non-muscle invasive urothelial cancers, management with Transurethral Resection of Bladder Tumour (TURBT) and cystoscopic surveillance is usually done. In native kidney UTUC, the surgery of choice is radical nephroureterectomy. Notably, 41 to 53% of post-transplant patients developed contralateral UTUC.[43] Hence, surveillance is equally if not more important in TXP patients. In transplanted kidney UTUC, the treatment is total transplant nephroureterectomy or transplant preserving surgery.

**Intravesical BCG**

Bacillus Calmette–Guérin (BCG), a live attenuated strain of Mycobacterium bovis, is used as a form of intravesical therapy that has shown excellent outcomes in reducing tumour

**Table 3.** Epidemiological data review of urothelial carcinoma in kidney transplant patients compared with the general population.

| | General population | Kidney transplantation |
|---|---|---|
| Bladder UC<br>Standardised incidence rate<br>(/100,000) | Bladder – Incidence 0.02% | 3.15 (ESRD 2.51)<br>-1.4 (1.3-1.5) USRDS<br>-1.5 (1.4-1.7) EDTA<br>- 4.8 (3.6-6.2) ANZDATA<br>- 14.74 (ASIAN) |
| Risk factors | Male, age, smoking, aristolochic acid<br>(Geographic) | +Lifelong immunosuppression<br>+ BKV (RR11.6)<br>+ HPV Infection |
| At presentation | MIBC 24%<br>Late stage 15% | MIBC 37%, (ESRD 33%)<br>Late stage 34%<br>Bladder 92% (UTUC 8%)<br>Median time from transplantation 4.5 years |
| Prognosis | | Survival worse<br>5 year CSS – 50%<br>10 year CSS – 0% |

MIBC = muscle-invasive bladder cancer, ESRD = send-stage renal disease, BKV = BK virus, HPV = human papilloma virus, UTUC = upper tract urothelial carcinoma, CSS = cancer-specific survival.

recurrence and mortality.[44] In terms of general population management of non-muscle invasive urothelial carcinoma (NMIUC), this is the standard of care for adjuvant therapy in conjunction with TURBT. However, in immunosuppressed patients such as kidney TXPs, this treatment is cautioned against, and even considered a contraindication due to the increased risk of sepsis and severe morbidity.[45] Mainly, BCG cystitis has been reported to be 20 times more common in transplant patients.[46] In Palou's study of intravesical BCG used in management of 3 renal transplant patients with high-grade superficial bladder cancer and carcinoma-in-situ (CIS), 1 out of the 3 patients developed disease recurrence at 10 months and underwent radical cystectomy.[47] However, overall safe administration of intravesical BCG was recorded. Here, the prophylactic antibodies used were a 3 day course of Isoniazid and Rifampicin. Similarly, in Tomaszewski's study, overall possible but judicious use of intravesical BCG in TXPs is concluded, with the use of prophylactic antibodies and maintenance of a high clinical surveillance for BCG related sepsis.[48] In their study, initially reported 7 months of T1 recurrence and 2 cases of CIS recurrence at 12 and 18 months, although these 3 patients were all free of recurrence subsequently. Notably, the prophylaxis of choice here was Ciprofloxacin.

Herr's study had the biggest group of 12 kidney TXPs. It found 6 out of 12 progressions and 11 out of 12 recurrences.[49] Prophylaxis given was not reported. For TXPs who were BCG treated, recurrence free survival rates and progression free rates were lower compared to other immunosuppressed patients with other cancers or with autoimmune diseases.

The use of intravesical BCG in the management of UC in transplant patients can be advocated with great caution. Close monitoring of transplant patients following its use for potential toxicity is important, or consider other adjuvant therapies such as intravesical Mitomycin.

**Management of UC in Transplanted Kidneys or Ureters**

With less than 50 case reports in literature, its incidence is placed at 0.15 to 0.18%. When dealing with UC in the transplant kidney, two treatments would be considered: transplant preserving surgery and total transplant nephroureterectomy (TNU).

In many studies, TNU remains the primary intervention. Similarly in non-transplant patients, the EAU guidelines recommend radical nephroureterectomy as gold-standard management of localised UC.[50] Caveats include the possible indication of kidney-sparing ureteric segmental resection in low-grade UC tumours. Unlike RCC, UC is considered a more aggressive cancer with a poor prognosis and nephro-sparing surgery should only be considered in very carefully selected cases. Olsburg et al. presented four cases of UC of the transplanted ureter treated with segmental ureterectomy.[51] 3 out of 4 patients had recurrence and two eventually succumbed to their disease, demonstrating the hazards of preserving the transplanted kidney.

The focus of management must be on oncological care rather than graft preservation. This means, TNU may be preferable to segmental resection.

**Table 4.** A summary of studies mentioned in this review article regarding intravesical BCG.

| Authors | N | Prophylaxis | Follow up/ months | BCG sepsis | Outcomes |
|---|---|---|---|---|---|
| Palou et al. | 3 (2 T1HG,1 CIS) | 3-day course of isoniazid and rifampicin | 17-60 | Nil. | 1 patient CIS recurrence at 10 months --> radical cystectomy |
| Tomaszewski et al. | 3 CIS, 1 T1 LG | Ciprofloxacin x 1 dose | 36-84 | Nil. | T1 recurrence 7 months, 2 CIS recurrence at 12 and 18 months, BCG course repeated, all free of recurrence subsequently |
| Herr et al. | 45 (12 renal transplantations) | Unknown | 40 (12-72) | Nil. | 6 out of 12 progress<br>11 out of 12 recurrence |

T = tumor, HG = high grade, CIS = carcinoma in-situ, LG = low grade, BCG = Bacillus Calmette–Guérin.

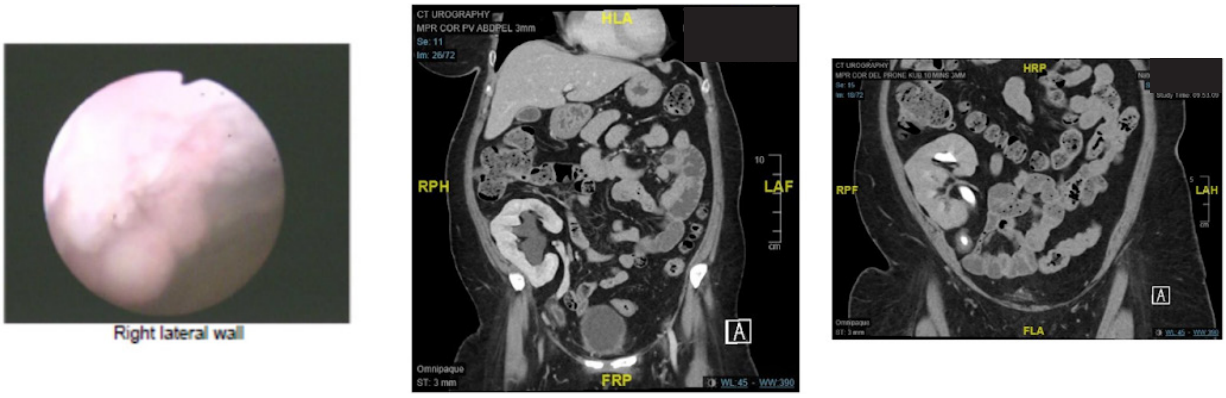


**Figure 3.** Bladder cancer on cystoscopy at transplant ureter-bladder anastomosis (left); CT scans (April 2018) depicting a hydronephrotic transplant kidney with dilated ureter to level proximal to anastomosis, where tumour was found (right).

Figure 3 is a case of a 54 year old Chinese lady who underwent a kidney transplant in 2005. With a background of BKV nephropathy, she presented with gross haematuria. Investigations reviewed a muscle invasive urothelial cancer at the transplant ureter-bladder anastomosis. A TNU was performed, together with a radical cystectomy and pelvic lymph node dissection in 2018. Histology confirmed the diagnosis of muscle-invasive bladder cancer (MIBC) and transitional cell carcinoma (TCC) in the transplanted ureter. There were no lesions in the transplanted kidney and no nodal spread. In view of the node negative disease and R0 resection, there was no adjuvant radiotherapy done. Patient was taken off immunosuppression and was two and a half years disease free as of February 2021. However, the psychological negative side effect of significant grief reaction to losing the transplant kidney remains and the patient suffers from depression with return to dialysis and loss of quality of life. This case reveals the significant challenge of managing UTUC in kidney TXPs where the dilemma of kidney preservation is balanced against life preservation.

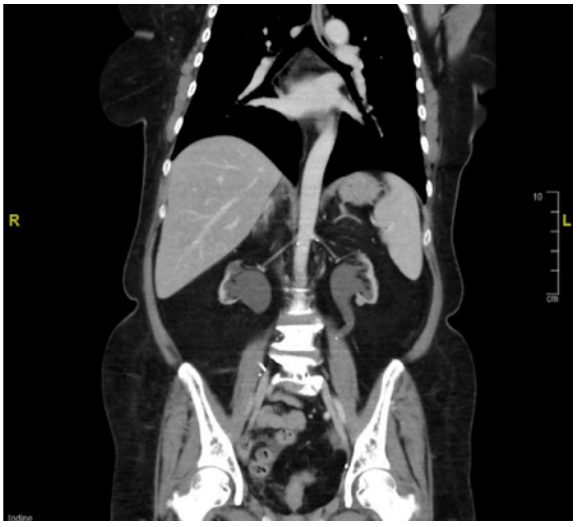


**Figure 4.** CT TAP of the same patient, disease-free (February 2021).

## Conclusion

Urological malignancies are increased in transplant patients when compared to both the general population and the ESRD population. Between the two types (RCC and UC) discussed in this article, RCC has better outcomes, especially at low stage and grade. Hence, screening for RCC in transplant patients can potentially allow for treatment with graft preservation by partial nephrectomy or ablation. Conversely, UC has significantly poorer prognosis. It is much less common, translating to limited evidence-based guidelines. However, for UC, oncological outcomes trump graft preservation, hence priority of management should be radical nephroureterectomy to optimise patient survival and recurrence rates instead. Research in this area should ideally be focused on prevention, especially with its links with BKV infection.

## Conflict of Interest

The authors declare no conflict of interest.

## References

1. Woo KT. Perspectives of end stage renal failure therapy in Singapore. Ann Acad Med Singap 1993; 22:393-400.
2. Soh P, Lim SM, Tan EC. Organ procurement in Singapore. Ann Acad Med Singap 1991;20:439-42.
3. Annual Report. Singapore: NRDO; 2021. Singapore Renal Registry Report.

4. Shern TKY. Renal transplantation at the Singapore General Hospital: a miracle in the making over 50 years. Proceedings of Singapore Healthcare. 2020; 29:245-51.
5. Tonelli M, Wiebe N, Knoll G, Bello A, Browne S, Jadhav D, et al. Systematic review: kidney transplantation compared with dialysis in clinically relevant outcomes. Am J Transplant 2011;11:2093-109.
6. Chaudhry D, Chaudhry A, Peracha J, Sharif A. Survival for waitlisted kidney failure patients receiving transaplantation versus remaining on waiting list: systematic review and meta-analysis. BMJ 2022;37:e068769.
7. Au E, Wong G, Chapman JR. Cancer in kidney transplant recipients. Nat Rev Nephrol 2018;14:508-20.
8. Dahle DO, Skauby M, Langberg CW, Brabrand K, Wessel N, Midtvedt K. Renal Cell Carcinoma and Kidney Transplantation: A Narrative Review. Transplantation 2022;106:e52-63.
9. Goh A, Vathsala A. Native renal cysts and dialysis duration are risk factors for renal cell carcinoma in renal transplant recipients. Am J Transplant 2011;11:86-92.
10. Watschinger B, Budde K, Crepo M, Heemann U, Hilbrands L, Maggiore U. Pre-existing malignancies in renal transplant candidates-time to reconsider waiting times. Nephrol Dial Transplant 2019;34:1292-1300.
11. Boissier R, Hevia V, Bruins HM, Budde K, Figueiredo A, Lledó-García E, et al. The risk of tumour recurrence in patients undergoing renal transplantation for end-stage renal disease after previous treatment for a urological cancer: a systematic review. Eur Urol 2018;73:94-108.
12. Tsaur I, Karalis A, Probst M, Blaheta RA, Scheuermann EH, Gossmann J, et al. Development of urological cancers in renal transplant recipients: 30-year experience at the Frankfurt Transplant Center. Cancer Sci 2010;101:2430-5.
13. Abbas M, Pätzel M, Thurn A, Brinkmann OA, Bettendorf O. Incidental occurrence of papillary renal cell carcinoma in the native kidney with autosomal dominant polycystic kidney disease after renal transplantation: a case report. Mol Clin Oncol 2021;15:223.
14. Klatte T, Marberger M. Renal cell carcinoma of native kidneys in renal transplant patients. Curr Opin Urol 2011;21:376-9.
15. Demetrios M, Kiriaki K, Chrysoula A, Nikolaos G, John B, Spyridon V, et al. Renal cell carcinoma of native kidneys in renal transplant recipients: a single-center experience. Anticancer Res 2017;37:773.
16. Jarzemski P, Listopadzki S, Słupski P, Jarzemski M, Brzoszczyk B. Simultaneous bilateral native nephrectomy by retroperitoneal approach. Int Braz J Urol 2020;46:538-44.
17. Park KH, Yoon JA, Kim HS, Kim H, Park SK, Kim YH, et al. Clinical features and outcomes in kidney transplant recipients with renal cell carcinoma: a single-center study. Kidney Res Clin Pract 2019;38:517-24.
18. European Renal Best Practice Transplantation Guideline Development Group. ERBP Guideline on the Management and Evaluation of the Kidney Donor and Recipient. Nephrol Dial Transplant 2013;28:ii1-71.
19. Ljungberg B, Albiges L, Bedke J, Bex A, Capitanio U, Giles RH, et al. EAU Guidelines on Renal Cell Carcinoma [Internet]. [cited 2023 July 15]:1-99. Available from: https://d56bochluxqnz.cloudfront.net/documents/full-guideline/EAU-Guidelines-on-Renal-Cell-Carcinoma-2023.pdf
20. Lu J, Tay HW, Wu MW, Rahman L, Tiong HY. Outcomes of radical nephrectomyfor end stage renal failure (ESRF) patients with renal Cell carcinoma (RCC) Abstracts. BJU International 2014;113:1-37.
21. Chen K, Huang HH, Aydin H, Tan YH, Lau WK, Cheng CW, Yuen JS. Renal cell carcinoma in patients with end-stage renal disease is associated with more favourable histological features and prognosis. Scand J Urol 2015;49:200-4.
22. Graves A, Hessamodini H, Wong G, Lim WH. Metastatic renal cell carcinoma: update on epidemiology, genetics, and therapeutic modalities. Immunotargets Ther 2013;2:73-90.
23. Griffith JJ, Amin KA, Waingankar N, Lerner SM, Delaney V, Ames SA, et al. Solid Renal Masses in Transplanted Allograft Kidneys: A Closer Look at the Epidemiology and Management. Am J Transplant 2017;17:2775-81.
24. O'Connor E, Timm B, Lawrentschuk N, Ischia J. Open partial nephrectomy: current review. Transl Androl Urol 2020;9:3149-59.
25. Zhao H, Alam A, Soo AP, George AJT, Ma D. Ischemia-reperfusion injury reduces long term renal graft survival: mechanism and beyond. EBio Medicine 2018;28:31-42.
26. Battelli C, Cho DC. mTOR inhibitors in renal cell carcinoma. Therapy 2011;8:359-67.
27. Cuadrado-Payán E, Diekmann F, Cucchiari D. Medical Aspects of mTOR Inhibition in Kidney Transplantation. Int J Mol Sci 2022;23:7707.
28. Bermejo S, Bolufer M, Riveiro-Barciela M, Soler MJ. Immunotherapy and the spectrum of kidney disease: should we individualize the treatment? Front Med (Lausanne) 2022;9:906565.

29. Ardelt PU, Rieken M, Ebbing J, Bonkat G, Vlajnic T, Bubendorf L, et al. Urothelial cancer in renal transplant recipients: incidence, risk factors, and oncological outcome. Urology 2016;88:104-10.
30. Vajdic CM, McDonald SP, McCredie MR, van Leeuwen MT, Stewart JH, Law M, Chapman JR, Webster AC, Kaldor JM, Grulich AE. Cancer incidence before and after kidney transplantation. JAMA. 2006;296:2823-31.
31. Hickman LA, Sawinski D, Guzzo T, Locke JE. Urologic malignancies in kidney transplantation. Am J Transplant 2018;18:13-22.
32. Wang Y, Lan G, Peng F, Xie X. Cancer risks in recipients of renal transplants: a meta-analysis of cohort studies. Oncotarget 2018;9:15375-85.
33. Hosain GMM, Khan MM, Amiel GE, Lerner SP, Latini DM, Chen GJ. Racial/Ethnic Differences in Upper-Tract Urothelial Cancer. Rthn Dis 2012;22:295-301.
34. Miao Y, Everly JJ, Gross TG, Tevar AD, First MR, Alloway RR, et al. De novo cancers arising in organ transplant recipients are associated with adverse outcomes compared with the general population. Transplantation 2009;87:1347-59.
35. Vajdic CM, McDonald SP, McCredie MR, van Leeuwen MT, Stewart JH, Law M, et al. Cancer incidence before and after kidney transplantation. JAMA 2006;296:2823-31.
36. Chen CH, Dickman KG, Moriya M, Zavadil J, Sidorenko VS, Edwards KL, et al. Aristolochic acid-associated urothelial cancer in Taiwan. Proc Natl Acad Sci U S A 2012;109:8241-6.
37. Liu S, Chaudhry MR, Berrebi AA, Papadimitriou JC, Drachenberg CB, Haririan A, et al. Polyomavirus replication and smoking are independent risk factors for bladder cancer after renal transplantation. Transplantation 2017;101:1488-94.
38. van Aalderen MC, Heutinck KM, Huisman C, ten Berge IJ. BK virus infection in transplant recipients: clinical manifestations, treatment options and the immune response. Neth J Med 2012;70:172-83.
39. Viswesh V, Yost SE, Kaplan B. The prevalence and implications of BK virus replication in non-renal solid organ transplant recipients: A systematic review. Transplant Rev (Orlando) 2015;29:175-80.
40. Wang Y, Yan S, Liu Y, Yan Z, Deng W, Geng J, et al. Dynamic viral integration patterns actively participate in the progression of BK polyomavirus-associated diseases after renal transplantation. Am J Transplant 2023;23:1694-1708.
41. Ortega RMM, Wolff DJ, Schandl CA, Drabkin HA. Urothelial carcinoma of donor origin in a kidney transplant patient. J Immunother Cancer 2016;4:63.
42. Fedeli U, Fedewa SA, Ward EM. Treatment of muscle invasive bladder cancer: evidence from the national cancer database, 2003 to 2007. J Urol 2011;185:72-8.
43. Tsaur I, Karalis A, Blaheta R, Juenge E, Vallo S, Probst M, et al. Transitional cell carcinoma of the native urinary tract after kidney transplantation: recommendations following a long-term retrospective analysis. Am J Med Sci 2011;341:478-83,
44. Jiang S, Redelman-Sidi G. BCG in Bladder cancer immunotherapy. Cancers (Basel) 2022;14:3073.
45. Prabharasuth D, Moses KA, Bernstein M, Dalbagni G, Herr HW. Management of bladder cancer after renal transplantation. Urology 2013;81:813-9.
46. Deresiewicz RL, Stone RM, Aster JC. Fatal disseminated mycobacterial infection following intravesical bacillus Calmette-Guerin. J Urol 1990;144:1331-3; discussion 1333-4.
47. Palou J, Angerri O, Segarra J, Caparrós J, Guirado L, Diaz JM, et al. Intravesical bacillus Calmette-Guèrin for the treatment of superficial bladder cancer in renal transplant patients. Transplantation 2003;76:1514-6.
48. Tomaszewski JJ, Larson JA, Smaldone MC, Hayn MH, Jackman SV. Management of Bladder Cancer following Solid Organ Transplantation. Adv Urol 2011;2011:256985.
49. Herr HW, Dalbagni G. Intravesical bacille Calmette-Guérin (BCG) in immunologically compromised patients with bladder cancer. BJU Int 2013;111:984-7.
50. Rouprêt M, Gontero P, Birtle A, Compérat EM, Dominguez-Escrig JL, Liedberg F, et al. EAU Guidelines on Upper Urinary Tract Urothelial Carcinoma [Internet]. 2023 [cited 2023 July 15]:1-44. Available from: https://d56bochluxqnz.cloudfront.net/documents/full-guideline/EAU-Guidelines-on-Upper-Urinary-Tract-Urothelial-Carcinoma-2023.pdf
51. Olsburgh J, Zakri R, Horsfield C, Collins R, Fairweather J, O'Donnell P, Koffman G. TCC in transplant ureter-When and When not to preserve the transplant kidney. Am J Transplant 2016;16:704-11.