

NEPHRON SPARING PARTIAL NEPHRECTOMY FOR RENAL CELL CARCINOMA IN TRANSPLANTED KIDNEY AFTER SIMULTANEOUS PANCREAS- KIDNEY TRANSPLANTATION - FIRST REPORT OF TWO CASES

Georg Ebeling¹, Tomas Urbonas¹, Maria Soares², Ra'ed Haddad³,
Mark Sullivan³, Venkatesha Udupa¹

¹ Oxford Transplant Centre, Oxford University Hospitals NHS Foundation Trust, Oxford, UK; ² Department of Cellular Pathology, Oxford University Hospitals NHS Foundation Trust, Oxford, UK; ³ Department of Urology, Oxford University Hospitals NHS Foundation Trust, Oxford, UK

Summary

Simultaneous pancreas-kidney transplantation (SPK) is one of the treatment options for type 1 diabetes mellitus with end-stage renal failure. Solid organ transplant recipients are more susceptible to developing post-transplant cancers, including renal cell carcinoma compared to the general population. While the incidence of renal cell carcinoma is up to 10 times higher in kidney-only transplant recipients, reports of renal cell cancers in renal grafts after SPK transplantation are rare and successful nephron sparing partial nephrectomy has not yet been reported in literature. We present herein the case report of two patients, aged 47 and 54 years old, who underwent a successful partial nephron-sparing graft nephrectomy for clear cell and papillary renal cell carcinoma ten and fourteen years after his SPK transplant respectively. Both patients made a full recovery after surgery and maintained good renal function in the respective 12-month and 9-month postoperative period.

Key words: renal cell carcinoma (RCC), renal cancer, simultaneous pancreas-kidney transplant (SPK), partial nephrectomy, nephron-sparing nephrectomy

Received: December 9, 2024
Accepted: May 27, 2025

Correspondence

Georg Ebeling

E-mail: georg.ebeling@nds.ox.ac.uk

How to cite this article: Ebeling G, Urbonas T, Soares M, et al. Nephron sparing partial nephrectomy for renal cell carcinoma in transplanted kidney after simultaneous pancreas-kidney transplantation - First report of two cases. EJT 2024;2:128-134. <https://doi.org/10.57603/EJT-890>

© Copyright by Pacini Editore Srl



OPEN ACCESS

This is an open access article distributed in accordance with the CC-BY-NC-ND (Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International) license. The article can be used by giving appropriate credit and mentioning the license, but only for non-commercial purposes and only in the original version. For further information: <https://creativecommons.org/licenses/by-nc-nd/4.0/deed.en>

Abbreviations

AKI: Acute Kidney Injury
CCRCC: Clear Cell Renal Cell Carcinoma
CIA: Common Iliac Artery
CIV: Common Iliac Vein
CT: Computed Tomography
DBD: Donation after Brain(stem) Death
[F]: French
HD: Haemodialysis
H&E: Hematoxylin and Eosin Staining
ISUP: International Society of Urological Pathology
KTx: Kidney Transplantation
MDT: Multi-Disciplinary Team
MMF: Mycophenolate Mofetil

NSS: Nephron-Sparing Surgery
 PRCC: Papillary Renal Cell Carcinoma
 PVD: Peripheral Vascular Disease
 RCC: Renal Cell Carcinoma
 SBO: Small Bowel Obstruction
 SOT: Solid Organ Transplantation
 SPK: Simultaneous Pancreas-Kidney transplantation
 T1DM: Diabetes Mellitus Type 1
 Tx: Transplant (operation)
 UICC: Union for International Cancer Control
 WIT: Warm Ischaemia Time

INTRODUCTION

Simultaneous pancreas-kidney (SPK) transplantation is one of the treatment options for type 1 diabetes mellitus (T1DM) and in selected cases type 2 diabetes mellitus (T2DM) and end-stage renal failure¹. Solid organ transplant (SOT) programmes have become increasingly successful over the last decades, however, prolonged graft function and patient survival after SOT require recipients to take immunosuppressive agents for an extended time, which makes them more susceptible to developing post-transplant cancers. It is assumed that the overall risk of cancer onset following SOT is up to four times higher than in the general population². It is predicted that cancer may eventually become the leading cause of death after SOT³. Renal cell carcinoma (RCC), accounts for up to 90% of all kidney malignancies and mostly presents as clear cell RCC in 75%⁴⁻⁶. After SOT, the risk of RCC is threefold higher in thoracic or liver transplant recipients and up to 10 times higher in kidney transplant (KTx) recipients^{4,7}. While reports of cancer after SPK transplantation are relatively rare, the overall incidence of malignancy after pancreas and or kidney transplantation in diabetics has been reported to be as high as 12%^{8,9}. The commonest tumours are non-melanoma skin cancers (NMSC) and post-transplant lymphoproliferative disorder (PTLD). Seventy-five percent of RCC in non-transplant patients present with localised disease without metastatic spread; hence, radical or partial nephrectomy (NSS, nephron-sparing surgery) or ablation are the preferred treatment options. NSS and ablation provide reduced long-term morbidity due to their nephron-saving nature¹⁰ by avoiding long-term dialysis and its consequences. We report a summary of two rare cases of patients with a papillary and a clear cell RCC in a kidney graft after SPK transplantation, which were both successfully resected with preservation of renal function. Both patients' details are summarized in Table I.

CASE 1. NEPHRON-SPARING SURGERY FOR PAPILLARY RENAL CELL CARCINOMA 14 YEARS AFTER SIMULTANEOUS PANCREAS-KIDNEY TRANSPLANTATION

Patient 1 was a 54-year-old male with adult-onset T1DM diagnosed at the age of 24 years. Further comorbidities included hypertension, peripheral vascular disease (PVD), diabetic retinopathy and myocardial infarction necessitating coronary artery bypass grafting. The patient had been on haemodialysis (HD) for two years. In 2008, he successfully underwent an SPK transplant from a 43-year-old heart-beating donor with a human leukocyte antigen (HLA) mismatch of 2-2-1. He was given alemtuzumab on induction and later commenced on dual immunosuppressive maintenance with tacrolimus and mycophenolate mofetil (MMF). During recovery, the patient experienced two episodes of small bowel obstruction (SBO) secondary to adhesions, necessitating explorative laparotomies at three weeks and nine months postoperatively. He was referred to his local renal unit for long-term follow-up with good primary renal and pancreatic function and baseline creatinine levels of 139 mmol/L.

Fourteen years later, he underwent an investigation for deteriorating renal graft function. A computed tomography (CT) scan revealed both a cystic upper pole lesion measuring 4.3 cm without any enhancement, and an interpolar complex cystic lesion with a partial solid component measuring 3.1 cm with enhancement on arterial phase scanning in its superior portion (Fig. 1). The native kidneys were described as bilaterally atrophic. No evidence of metastatic disease was seen. The biopsy of the complex cystic lesion confirmed that it was papillary RCC (PRCC), while the imaging suggested that the upper pole cystic lesion was benign. After the review of the case in a multidisciplinary team (MDT) meeting, it was decided that open NSS would be performed as ablation was not feasible due to the size and proximity of the lesion to the hilum. Surgery was performed by urology and transplant consultant surgeons as a joint case. After midline laparotomy and adhesiolysis, the transplanted kidney was fully mobilised. The right common iliac artery (CIA) distal to take off of the Y graft of pancreas, right common iliac vein (CIV) and internal iliac vessels were dissected out and slung as proximal vascular control. Parallel to the inguinal ligament, a second incision was made in the right groin to control and sling the right femoral artery and vein as distal vascular control. Femoral distal control was necessary as distal external iliac vessels could not be dissected safely due to post operative fibrosis. The tumour was visualised and demarcated using an intraoperative ultrasound scan. The upper pole cyst was also rescanned and had benign appearances.

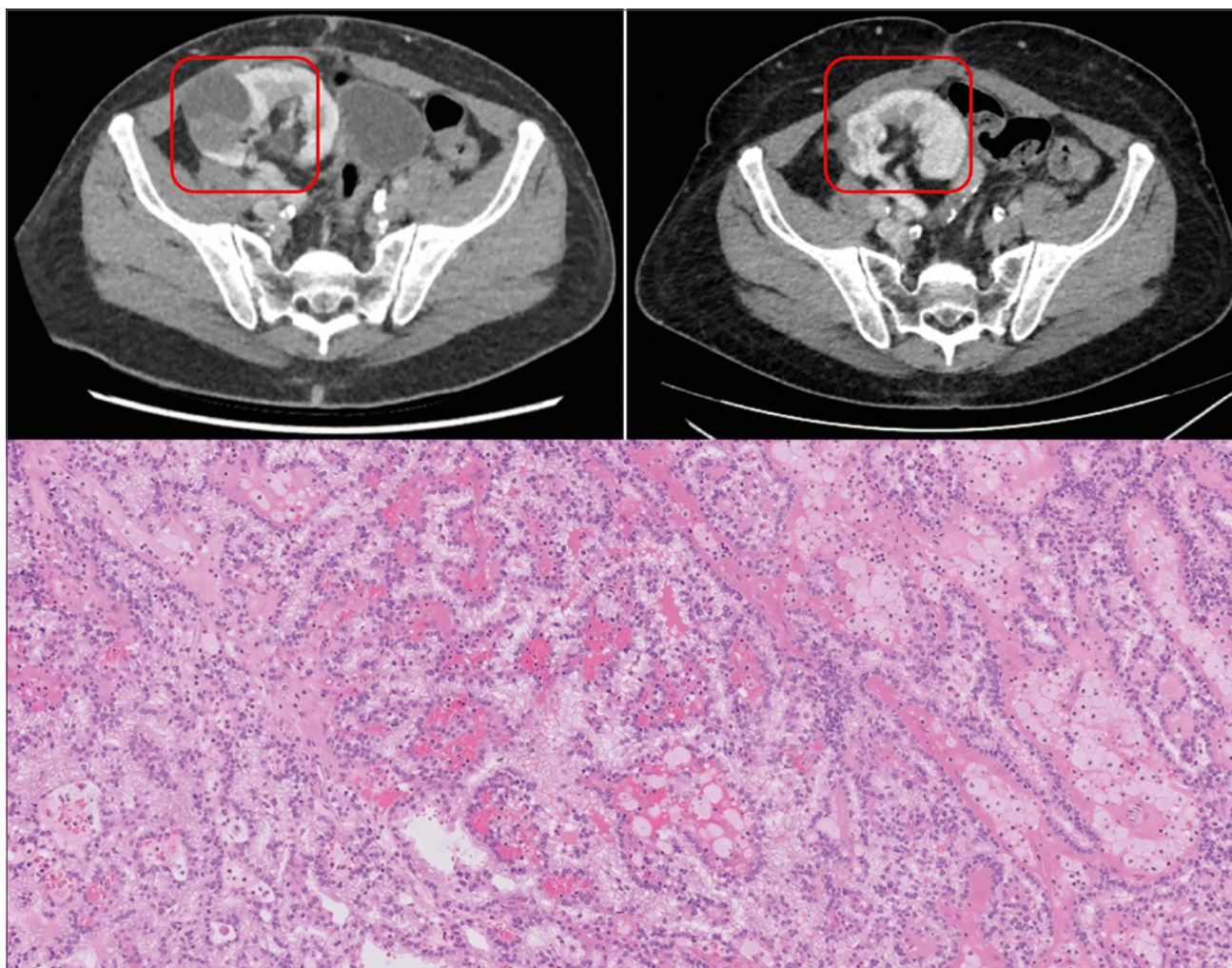


Figure 1. Patient 1: preoperative kidney tumour finding and post-operative results. A preoperative CT scan (**top left**) showed an interpolar complex cystic lesion that demonstrated a partial solid component with enhanced arterial phase scanning in its superior portion. A 12-month post-operative CT scan (**top right**) after the partial nephrectomy showed the allograft kidney without any evidence of local tumour recurrence. **Bottom:** a papillary renal cell carcinoma (PRCC), previously classified as Eble Type I, showing well-formed papillae lined by cuboidal to columnar cells, with a pale cytoplasm. The nuclei show visible nucleoli at this magnification, akin to ISUP Grade 3. The papillae contain numerous foamy cells. H&E x10.

The right CIA and CIV along with internal iliac vessels were clamped proximally, and the right femoral artery and vein were clamped distally. The renal mass was excised with the cyst intact, while one calyx was opened and closed with a 4-0 polydioxanone suture. Significant venous bleeding was controlled with multiple interrupted 5-0 prolene sutures. Despite a 1.5-litre blood loss, no blood transfusions were required due to use of cell salvage for perioperative blood conservation. The duration of the warm ischaemia time (WIT) was 32 minutes. A 20 F [French] Robinson drain was placed lateral to the renal bed and the incision was closed. The histopathological assessment of the excised tumour and one common iliac lymph node confirmed a

PRCC ISUP (International Society of Urological Pathology) grade 3 pT1a pN0 (UICC TNM 8th Ed.) with negative margins (Fig. 1).

Postoperatively, the patient was admitted to intensive care and stepped down to the ward the following day. A postoperative CT showed no graft pancreatitis and only minimal fluid collection around the graft kidney. Eleven days after surgery, the patient was discharged with a creatinine level of 160 $\mu\text{mol/L}$ and normal blood glucose levels. A repeated CT scan six and twelve months postoperatively revealed no evidence of local or distant disease recurrence (Fig. 1). After a 18-month follow-up, the renal function was stable, with a creatinine level of 156 $\mu\text{mol/L}$.

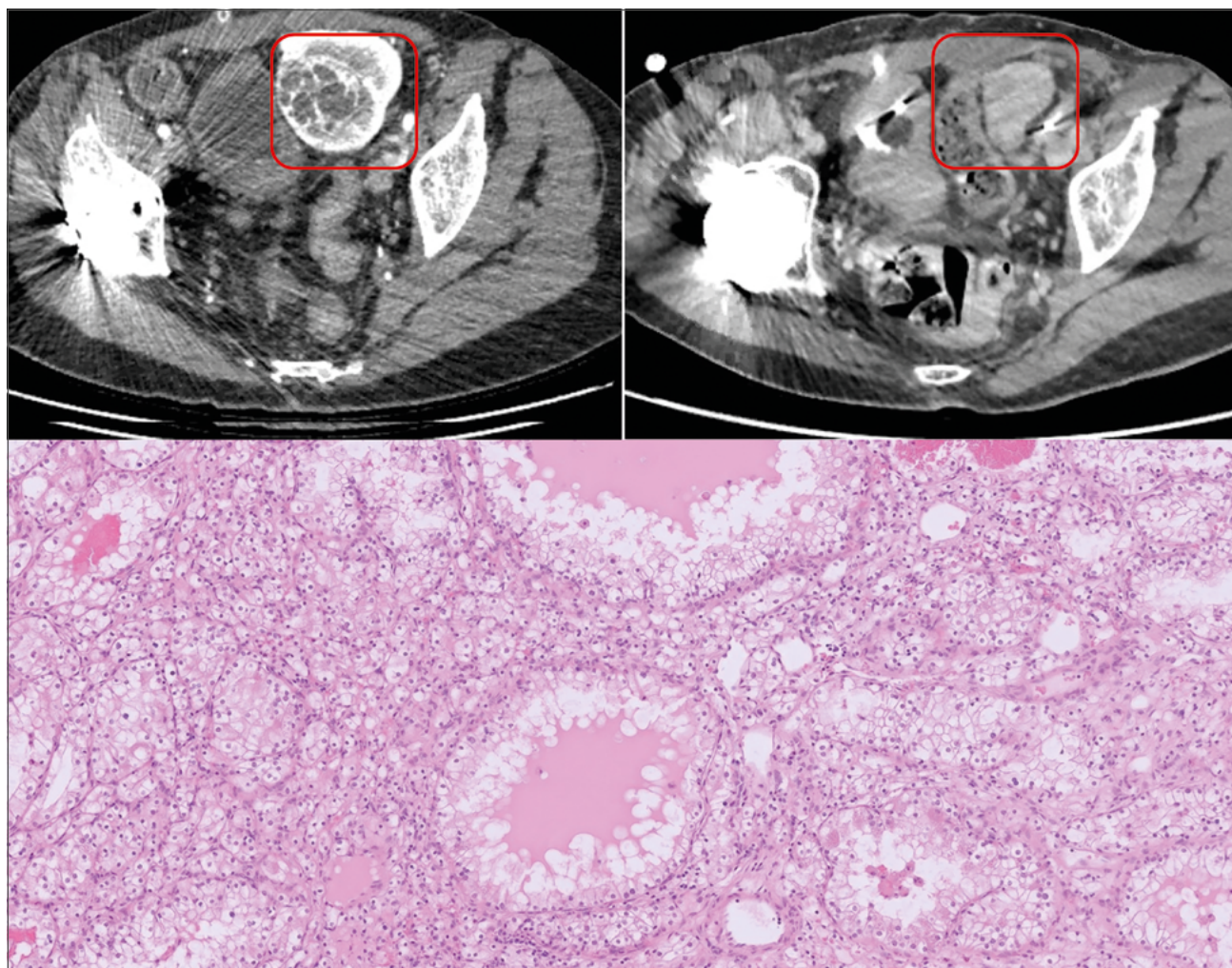


Figure 2. Patient 2: preoperative kidney tumour finding and post-operative results. A preoperative CT (**top left**) scan showed a mass at the lower pole of transplanted kidney. A 3-month post-operative CT scan (**top right**) after the partial nephrectomy showed the lower pole of the allograft kidney without any evidence of local tumour recurrence. **Bottom:** a clear cell renal cell carcinoma (CCRCC). There are clear cells with nuclear atypia, akin to ISUP Grade 2, in solid, tubular, cystic and nested arrangements. There are no visible nucleoli at this magnification. H&E x10.

The endocrine function of the pancreas remained intact.

CASE 2. NEPHRON-SPARING SURGERY FOR CLEAR CELL RENAL CELL CARCINOMA 10 YEARS AFTER SIMULTANEOUS PANCREAS-KIDNEY TRANSPLANTATION

The second case was a 47-year old male with adult-onset T1DM diagnosed at the aged 27 years. Further comorbidities included hypertension, blindness, long-term suprapubic catheterisation for neurogenic bladder, Perthes' diseases, hip replacement, severe depression

with attempted suicide 2003 and ongoing medical treatment and cannabis dependence. He had been on HD for three years. In 2014, he successfully underwent an SPK transplant from a 40-year-old heart-beating donor with an HLA mismatch of 1-1-2. He was given alemtuzumab on induction and later commenced on dual immunosuppressive maintenance with tacrolimus and MMF. Three months post-operatively, he experienced one episode of SBO secondary to adhesions, necessitating an explorative laparotomy and small bowel resection. He was referred to his local renal unit for long-term follow-up with excellent primary renal and pancreatic function and baseline creatinine levels of 80 $\mu\text{mol/L}$ (GFR > 90). Ten years later, he was diagnosed with a 4.3 cm biopsy proven clear cell RCC (CCRCC) on the transplant graft which was initially picked

Table 1. Patient and case summary.

	Patient 1	Patient 2
Age at adult T1DM diagnosis	24 years	27 years
Type of Tx, recipient age at Tx	SPK, 40 years	SPK, 37 years
Donation type	DBD	DBD
Age & Gender of Donor	43 years, male	40 years, male
HLA MM	2 - 2 - 1	1 - 1 - 2
Immunosuppression: induction	Alemtuzumab	Alemtuzumab
Immunosuppression: long-term	Tacrolimus, MMF	Tacrolimus, MMF
Time between Tx and RCC diagnosis (tumour operation)	14 years (14 years)	8 years (10 years)
Patient age at tumour operation	54 years	47 years
BMI	26 kg/m ²	21 kg/m ²
Relevant comorbidities	Hypertension, retinopathy, PVD, myocardial infarction, CABG, reduced exercise tolerance	Hypertension, blindness, neurogenic bladder, subarachnoid haemorrhage, depression, previous suicide attempt
Pre-operative RCC diagnostics	CT, kidney biopsy	CT, kidney biopsy
Tumour location	Interpolar	Lower pole
Indication for Surgery discussed in MDT	Yes	Yes
WIT	32 min	25 min
Intraoperative blood loss	1.5 L	2 L
Intraoperative cell salvage	Yes	Yes
Blood transfusion needed	No	No
Insulin Requirements	No	No
Baseline creatinine (eGFR) before tumour operation	139 mmol/L (49)	80 mmol/L (> 90)
Post-operative AKI	Yes	Yes
Post-operative dialysis required	No	No
Creatinine (eGFR) upon Discharge	161 mmol/L (41)	136 mmol/L (53)
Follow-up Creatinine (eGFR)	156 mmol/L (42) After 18 months	178 mmol/L (38) After 9 months
Duration of hospital admission	12 days	12 days
Tumour entity	ISUP Grade 3 Papillary RCC pT1a pN0	ISUP Grade 2 Clear Cell RCC pT1a pN0
Adjuvant therapy	No	No

up two years earlier but kept under initial surveillance. He was referred to our centre for further management. Noteworthy, he recovered from a subarachnoid hemorrhage in 2022 and he had to undergo venesection prior to surgery in view of his polycythemia. The lesion was too large for ablation treatment based on current guidelines. Surgery was performed by urology and transplant consultant surgeons as a joint case. After midline laparotomy and adhesiolysis, the transplanted kidney was fully mobilised. To gain complete vascular control left distal CIA and proximal CIV, left proximal IIA, distal IIV, EIA and vein distal to renal vessel anastomosis were dissected looped and clamped prior to excision of the tumour. The tumour

was visualised on the lower pole and demarcated using an intraoperative ultrasound scan. The renal mass was completely excised and an opened calyx was closed 4-0 PDS during excision. Post resection bleeding from the renal parenchyma controlled with multiple interrupted 5-0 prolene sutures. Despite a 2-litre blood loss, no blood transfusion was required as we used cell saver. WIT was 25 minutes. A 20F Robinson drain was placed lateral to the renal bed and the incision was closed. A 5F 12 cm JJ stent was placed via flexible cystoscopy. The histopathological assessment of the excised tumour and one common iliac lymph node confirmed a CCRCC ISUP grade 2 CCRCC pT1a pN0 (UICC TNM 8th Ed.) with negative margins (Fig. 2).

After a brief recovery period on the ICU, the patient was transferred back to the ward. After surgery, creatinine levels increased to 182 $\mu\text{mol/l}$ but improved with fluid resuscitation, however it had not returned to preoperative values. Apart from a severe delirium managed with psychiatric input and interim olanzapine, the patient's stay was unremarkable, and he was discharged with a creatinine level of 136 $\mu\text{mol/L}$ after 12 days. After a 9-month follow-up, the renal function was relatively stable, with a creatinine level of 178 $\mu\text{mol/L}$ and preserved function of the pancreas graft. A repeated CT scan three months postoperatively revealed no evidence of local or distant disease recurrence (Fig. 2).

DISCUSSION

To the best of our knowledge, we report the first two cases of a successful partial nephrectomy of a kidney graft RCC in high-risk patients after SPK transplantation. Following renal transplantation up to 90% of RCCs are found in the native kidneys². RCC in renal grafts presents mostly as clear-cell RCC (46%) or papillary RCC (42%), and the incidence is approximately 0.5%^{11,12}. Similar SPK studies have not yet included any RCC cases of the renal graft^{8,9,11-13}.

Localised RCC in a graft kidney can be treated with open total/radical or partial nephrectomy or percutaneous ablative techniques, such as radiofrequency or cryoablation. Griffith et al. identified 56 relevant studies in their recent systematic review examining the epidemiology and management of graft renal masses. NSS was performed in 67.5% of the patients, while the remaining were treated with radical nephrectomy (19.5%), percutaneous radiofrequency ablation (10.4%) or percutaneous cryoablation (2.4%)¹⁴. Cancer recurred in 3.6% of patients following a partial nephrectomy in transplanted kidneys, which is comparable to 3.0% of individuals following a native partial kidney nephrectomy. Although percutaneous ablative techniques are less invasive and have reduced morbidity, the prevalence of local recurrence rates in graft kidneys is as high as 17.6%. Moreover, up to 7% of patients who undergo either NSS or ablative percutaneous procedures, return to dialysis^{14,15}.

In both cases due to substantial fibrosis in the renal hilar area including area around vascular anastomoses, it would be extremely difficult to safely dissect renal pedicle. Any attempt to dissect the renal pedicle in our opinion could compromise blood supply to the kidney leading to potential graft loss. We feel controlling inflow to kidney is better done with proximal and distal control of iliac vessels for the above-mentioned reasons as dissection is easier and safer in the area previously not entered to. There are reports in the literature where endovascular

control was achieved which demonstrates it is an option for such operations, however the disadvantage with described endovascular control is absence of renal venous outflow control which still results in increased blood loss¹⁶.

We did not attempt these cases using minimally invasive in particular robotic technique due to significant fibrosis after previous surgery. We feel that the tactile benefits at open surgery identifying vessels and anatomy outweigh any potential recovery benefits of keyhole robotic surgery. However, there are reports of robotic partial nephrectomy of tumours in renal allografts which demonstrates advantages in terms of blood loss and postoperative hospital stay¹⁷.

In addition to experienced surgical team for successful outcomes it is important to have an experienced anaesthetic team. In order to minimise ischemic injury to the grafts the aim is to maintain mean arterial pressure (MAP) of 80 mmHg throughout the procedure and immediate postoperative period. We endeavour to keep renal ischemia time during resection less than 30 minutes to minimise ischemic injury and to reduce blood loss. Routinely perioperative tranexamic acid is given intravenously and cell saver is used. Our intraoperative strategy to maintain MAP $\geq$ 80 mmHg is to maintain adequate preload and infusion volume management with close haemodynamic monitoring. Generally crystalloid or colloid infusions are administered before and during surgery to optimize intravascular volume and prevent hypotension. A liberal fluid strategy is often preferred to support renal perfusion, especially before clamping. Vasopressor support could be required with norepinephrine and vasopressin to maintain systemic vascular resistance and MAP. Ensuring an appropriate depth of anaesthesia avoids hypotension from excessive vasodilation or myocardial depression. Trendelenburg positioning could be required which can increase venous return. Use of arterial line monitoring provides real-time, beat-to-beat blood pressure and MAP tracking.

Our centre is nationally commissioned unit for complex partial nephrectomy and kidney auto transplantation therefore we have sufficient expertise with such complex situations.

The type of immunosuppressive therapy plays role in the development of post-transplant malignancies. Calcineurin inhibitors, such as cyclosporine and tacrolimus, have been associated with an increased risk of malignancies - particularly skin cancers and post-transplant lymphoproliferative disorder (PTLD) - due to their suppression of immune surveillance and promotion of oncogenic pathways. Azathioprine also elevates the risk of skin cancer through photosensitizing effects, whereas mycophenolate mofetil is generally considered less tumorigenic. In contrast, mammalian target of rapamycin (mTOR) inhibitors like

sirolimus and everolimus possess antiproliferative and antiangiogenic properties and are associated with a reduced incidence of malignancies, making them a valuable alternative in high-risk patients. These differential effects underscore the importance of tailoring immunosuppressive regimens not only to prevent graft rejection but also to mitigate long-term cancer risk.

In our case series, which we believe to be the first report two complex patients with multiple comorbidities successfully underwent nephron-sparing surgery after simultaneous pancreas-kidney transplantation. The management of such unique cases should be carefully planned with multidisciplinary input.

CONCLUSIONS

Nephron sparing partial nephrectomy is challenging however appears to be feasible in selected cases of transplanted kidney RCC post SPK transplantation.

Conflict of interest statement

The authors declare no conflict of interest.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Author contributions

GE, TU: writing the manuscript; MS: reviewing the manuscript and taking micro images; RH: reviewing the manuscript; MS: operating surgeon and reviewing the manuscript; VU: operating surgeon and reviewing the manuscript.

Ethical consideration

Not applicable.

References

- Hopt UT, Drognitz O. Pancreas organ transplantation. Short and long-term results in terms of diabetes control. *Langenbecks Arch Surg* 2000;385:379-389. <https://doi.org/10.1007/s004230000124>
- Trofe J, Beebe TM, Buell JF, et al. Posttransplant malignancy. *Prog Transplant* 2004;14:193-200. <https://doi.org/10.1177/152692480401400304>
- Buell JF, Gross TG, Woodle ES. Malignancy after transplantation. *Transplantation* 2005;80(Suppl. 2):S254-S264. <https://doi.org/10.1097/01.tp.0000186382.81130.ba>
- Dahle DO, Skauby M, Langberg CW, et al. Renal cell carcinoma and kidney transplantation: a narrative review. *Transplantation* 2022;106:E52-E63. <https://doi.org/10.1097/TP.0000000000003762>
- Escudier B, Porta C, Schmidinger M, et al. Renal cell carcinoma: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up dagger. *Ann Oncol* 2019;30:706-720. <https://doi.org/10.1093/annonc/mdz056>
- Padala SA, Barsouk A, Thandra KC, et al. Epidemiology of renal cell carcinoma. *World J Oncol* 2020;11:79-87. <https://doi.org/10.14740/wjon1279>
- Au E, Wong G, Chapman JR. Cancer in kidney transplant recipients. *Nat Rev Nephrol* 2018;14:508-520. <https://doi.org/10.1038/s41581-018-0022-6>
- Pendon-Ruiz de Mier MV, Aguera ML, Navarro MD, et al. Prevalence and survival of cancer after pancreas-kidney transplantation. *Transplant Proc* 2018;50:669-672. <https://doi.org/10.1016/j.transproceed.2017.09.064>
- Martinenghi S, Dell'Antonio G, Secchi A, et al. Cancer arising after pancreas and/or kidney transplantation in a series of 99 diabetic patients. *Diabetes Care* 1997;20:272-275. <https://doi.org/10.2337/diacare.20.3.272>
- Jonasch E, Gao J, Rathmell WK. Renal cell carcinoma. *BMJ* 2014;349:G4797. <https://doi.org/10.1136/bmj.g4797>
- Ploussard G, Chambade D, Meria P, et al. Biopsy-confirmed de novo renal cell carcinoma (RCC) in renal grafts: a single-centre management experience in a 2396 recipient cohort. *BJU Int* 2012;109:195-199. <https://doi.org/10.1111/j.1464-410X.2011.10315.x>
- Tillou X, Guleryuz K, Doerfler A, et al. Nephron sparing surgery for De Novo kidney graft tumor: results from a multi-center national study. *Am J Transplant* 2014;14:2120-2125. <https://doi.org/10.1111/ajt.12788>
- Girman P, Lipar K, Kocik M, et al. Neoplasm incidence in simultaneous pancreas and kidney transplantation: a single-center analysis. *Transplant Proc* 2011;43:3288-3291. <https://doi.org/10.1016/j.transproceed.2011.09.011>
- Griffith JJ, Amin KA, Waingankar N, et al. Solid renal masses in transplanted allograft kidneys: a closer look at the epidemiology and management. *Am J Transplant* 2017;17(11):2775-2781. <https://doi.org/10.1111/ajt.14366>
- Van Poppel H, Da Pozzo L, Albrecht W, et al. A prospective, randomised EORTC intergroup phase 3 study comparing the oncologic outcome of elective nephron-sparing surgery and radical nephrectomy for low-stage renal cell carcinoma. *Eur Urol* 2011;59:543-552. <https://doi.org/10.1016/j.eururo.2010.12.013>
- Damodaran S, Ahmed A, Ekwenna O. Endovascular control during partial nephrectomy in a renal allograft. *Indian J Urol* 2022;38:227-229. https://doi.org/10.4103/iju.iju_38_22
- Banno T, Kobari Y, Fukuda H, et al. Comparing surgical outcomes between robot-assisted laparoscopic and open partial nephrectomy for allograft kidney tumors: a retrospective, single-center study. *BMC Surg* 2025;25:103. <https://doi.org/10.1186/s12893-025-02833-9>