

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.elsevier.com/locate/ajur

Review

Small renal masses in kidney transplantation: Overview of clinical impact and management in donors and recipients



Alberto Piana ^{a,b,*}, Iulia Andras ^c, Pietro Diana ^a, Paolo Verri ^{a,b},
 Andrea Gallioli ^a, Riccardo Campi ^{d,e}, Thomas Prudhomme ^f,
 Vital Hevia ^g, Romain Boissier ^h, Alberto Breda ^a,
 Angelo Territo ^a, on behalf of European Association of Urology
 (EAU) Young Academic Urologists (YAU) Kidney Transplantation
 Working Group, Arnhem, Netherlands

^a Department of Urology, Fundació Puigvert, Autònoma University of Barcelona, Spain

^b Department of Urology, San Luigi Gonzaga Hospital, University of Turin, Orbassano, Turin, Italy

^c Urology Department, Iuliu Hatieganu University of Medicine and Pharmacy and Municipal Hospital, Cluj-Napoca, Romania

^d Unit of Urological Robotic Surgery and Renal Transplantation, University of Florence, Careggi Hospital, Florence, Italy

^e Department of Experimental and Clinical Medicine, University of Florence, Florence, Italy

^f Department of Urology and Kidney Transplantation, Toulouse University Hospital, Toulouse, France

^g Hospital Universitario Ramon y Cajal. Alcala University, Instituto Ramon y Cajal de Investigación Sanitaria (IRYCIS), Madrid, Spain

^h Aix-Marseille université, service de chirurgie urologique et de transplantation rénale, CHU Conception, AP-HM, Marseille, France

Received 8 December 2021; received in revised form 24 March 2022; accepted 19 April 2022
 Available online 10 June 2022

KEYWORDS

Small renal mass;
 Renal cancer;
 Kidney
 transplantation;
 Nephron-sparing
 treatment

Abstract Kidney transplantation is the best replacement treatment for the end-stage renal disease. Currently, the imbalance between the number of patients on a transplant list and the number of organs available constitutes the crucial limitation of this approach. To expand the pool of organs amenable for transplantation, kidneys coming from older patients have been employed; however, the combination of these organs in conjunction with the chronic use of immunosuppressive therapy increases the risk of incidence of graft small renal tumors. This narrative review aims to provide the state of the art on the clinical impact and management of incidentally diagnosed small renal tumors in either donors or recipients. According to the

* Corresponding author. Department of Urology, San Luigi Gonzaga Hospital, University of Turin, Orbassano, Turin, Italy.
 E-mail address: alb.piana@gmail.com (A. Piana).
 Peer review under responsibility of Tongji University.

most updated evidence, the use of grafts with a small renal mass, after bench table tumor excision, may be considered a safe option for high-risk patients in hemodialysis. On the other hand, an early small renal mass finding on periodic ultrasound-evaluation in the graft should allow to perform a conservative treatment in order to preserve renal function. Finally, in case of a renal tumor in native kidney, a radical nephrectomy is usually recommended.

© 2022 Editorial Office of Asian Journal of Urology. Production and hosting by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

1. Introduction

Kidney transplantation (KT) is the best replacement treatment for end-stage renal disease (ESRD) and demonstrated solid advantages over hemodialysis in terms of survival and morbidity [1–3]. Currently, the imbalance between the number of patients on a transplant list and the number of organs available constitutes the crucial limitation of this approach. To overcome this limitation, nowadays, most grafts come from deceased donors who are usually over 60-year-old and the most common cause of death is a cerebrovascular event. Just in a few cases, when available, a living donor's graft is employed. The employment of donated kidneys coming from older patients in conjunction with the chronic use of immunosuppressive therapy increases the risk of incidence of graft tumors [3,4] that, in most of the cases, are diagnosed as asymptomatic incidental small renal tumors. Moreover, the incidental finding of a small renal mass (SRM) in a patient candidate for kidney donation constitutes another important issue in the transplantation decision-making process. This study aims to provide an overview of the current impact and the clinical management of incidentally diagnosed *de novo* SRMs in donors and in recipients.

2. Materials and methods

This is a narrative mini-review on the state of the art on the clinical impact and management of small renal incidentalomas in either donors or graft recipients. The research was restricted to articles published in the English language on PubMed database until September 2021 and largely based on the most updated evidence from European Association of Urology and the European Society of Medical Oncology guidelines. Among the keywords, we included "kidney", "tumor", "cancer", "renal cell carcinoma (RCC)", "transplant", "allograft", and "graft" (Fig. 1). All the articles were written in English, and tumor staging was defined according to the Union for International Cancer Control tumor, node, and metastasis (TNM) 2021 [5].

3. Management strategies in different clinical scenarios

Although KT constitutes the treatment of choice in case of ESRD [6], some issues are still needed to be considered in order to expand its indication.

Firstly, the high complexity and invasiveness of the procedure leads to major risk for all grade complications. In order to reduce the morbidities linked to the standard open

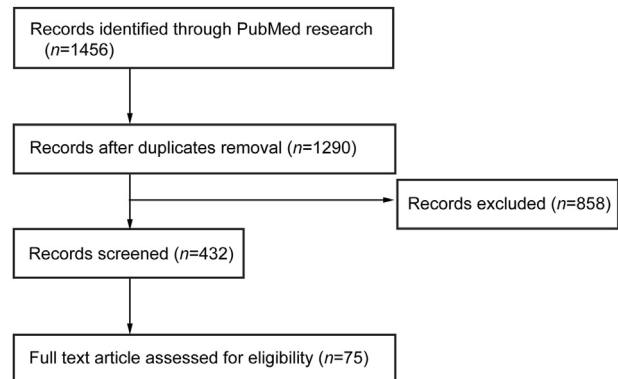


Figure 1 Flowchart of literature search.

approach, minimally-invasive surgical alternatives were introduced. The employment of these techniques led to a shorter hospital stay and a faster recovery, decreasing the use of analgesics and providing more satisfactory aesthetic results [7,8]; on the other hand, a longer ischemia time increases the risk of delayed graft function. To overcome these limitations, new surgical tools were introduced [9].

Secondly, the incidental finding of a SRM or a previous history of renal tumor in either recipients or donors is still a very debated issue and a priority research topic. The specific risk of RCC among transplanted patients is about 5–10 times increased compared to the general population [10]. In about 90% of the cases, it presents in native kidney and rarely in the graft [11]. The use of immunosuppressive drugs in patients undergoing KT increases overall 2–4 fold the risk for cancer compared to the general population, especially for ultraviolet radiation-related cancers (*i.e.*, skin cancer) and cancer associated to infections (*i.e.*, Epstein-Barr virus induced lymphoma).

In the general population, RCC accounts for around 2%–3% of all cancer, with the highest incidence in patients aged >60 years [12,13] with a rising incidence of SRMs, which consist in solid or complex cystic mass ≤ 4 cm. These masses are classified as pT1a according to TNM classification [5]. The size of the lesion and the histotype carry out the prognostic implications and define the treatment strategies according to the age and clinical conditions of the patients. The most common histotype of renal masses is clear cell RCC, accounting for around 90% of the cases [12].

In case of a patients neither scheduled for kidney donation nor transplantation, the recommended surgical treatment for a cT1a mass is minimally-invasive nephron-sparing surgery (NSS), considering its oncological safety and advantages in terms of overall survival (OS) over the radical nephrectomy

[14,15]. Other surgical alternatives are radiofrequency ablation, microwave ablation, or cryoablation, which are usually employed in patients with small cortical tumors with high surgical risk. In these cases, renal biopsy is strongly recommended to confirm malignancy and subtype [16,17]. In case of a frail patients with a short life expectancy and renal masses of <4 cm holding a previous renal biopsy, active surveillance may be considered as an option [18,19].

In case of patient who underwent KT, the epidemiology of renal tumor changes. Patients may develop kidney cancer in the native kidney after transplantation or more rarely in the transplanted graft. Moreover, another important issue is related to the incidental finding of SRMs in the living donor and the possibility and modality of transplantation. In these cases, it is important to assess diagnostic and therapeutic strategies in order to preserve graft function without compromising patient's survival.

3.1. SRM in donors

KT after *ex vivo* excision of small tumors has been reported since 1982 [20]. Incidental renal tumors are usually diagnosed during the surgical work-up prior to transplantation. Due to the low availability of organs, a careful case-by-case evaluation of donors with SRMs should be performed considering the low risk of recurrence of small and low-grade tumors. This risk should be balanced on the increased risk of mortality and morbidity for patients treated with dialysis in waiting list for transplantation [21].

The gold standard surgical management of a kidney with a SRM is, when feasible, an *ex vivo* tumor excision on the bench table with an oncological margin, a frozen section biopsy, subsequent renorrhaphy, and finally, transplantation [22].

Data of patients with SRM candidate to graft donation come from several case-reports, and a few systematic reviews and prospective non-randomized trials. Therefore, despite the promising data, only low-grade evidence is available.

Sener et al. [23] reported their results in 5 (3/5 RCC) living donor KTs of grafts with SRMs (<2.3 cm) incidentally detected during donor's diagnostic workup. The recipients were on dialysis and had a low life-expectancy. The tumor excision and subsequent renorrhaphy were performed on the bench table. A portion of the marginal tissue was sent for frozen-section analysis to confirm the absence of any residual tumor before proceeding with transplantation. The authors did not observe any tumor recurrence or metastasis, reporting a cancer-specific survival (CSS) of 100% with a median (range) follow-up of 15 (1–41) months [23]. Same treatment is provided for cT1a benign and malignant lesions, due to the very low recurrence rate in case of malignancy of any histotype [21].

In a prospective non-randomized trial from Ogawa et al. [24], 10 patients with low-medium surgical complexity SRMs according to nephrometry scores were selected for kidney donation to patients on dialysis and no tumor recurrence was reported at 32–58 months after surgery in either the recipients or the donors.

Although the lack of data from large cohorts, no difference in terms of functional or oncological outcomes was observed between living donors with incidental SRM and

deceased donors diagnosed for SRM during organ retrieval. Moreover, similar results were observed among different histological types [25].

A recent systematic review from Hevia et al. [22] on the use of kidneys with small renal tumors excised *ex vivo* reported that five-year OS was 92% and graft survival rates was 95.6%. The authors suggested that although with low-level evidence, kidneys with excised SRMs are an acceptable source of transplantation without compromising oncological outcomes and with similar functional outcomes to other donor kidneys. Their use should be mainly reserved to patients >60 years with a significant survival advantage by maximizing their residual renal function [26]. As suggested by Hevia et al. [22], preoperative biopsy may be useful to exclude Grade 4 RCC and a bench frozen section might be another key diagnostic tool to ensure a complete tumor resection.

3.2. Kidney transplant recipients with a history of pretransplant SRM

Patients with ESRD and cancer diagnosis before KT are considered a challenging group, due to the increased risk of posttransplant malignancies, graft loss, and decreased OS [27]. Previous history of cancer does not represent a contraindication to KT. However, the majority of centers recommend an arbitrary waiting time between no wait-time and 5 years, depending on the stage at diagnosis, as the risk of recurrence is considered the highest within the first 5 years after transplantation. According to the guidelines of the Canadian Society of Transplantation, patients with cT1 RCC require no waiting period between the tumor treatment and KT, whereas patients with a history of symptomatic RCC should wait at least 2 years and patients with locally-advanced disease should wait at least 5 years before KT [28].

Post-transplant malignancies most often occur in the same location as previous cancers, which suggest they may be in fact recurrences [29]. In kidney transplant recipients, the recurrence rate is the highest for kidney cancer of all malignancies [30]. A retrospective study on 258 kidney transplant recipients, in whom native nephrectomy was performed at the time of transplantation showed a rate of occult RCC of 4.7%. While the incidence of acute graft rejection was similar between the both groups (with or without occult RCC), a higher rate of RCC occurrence in the remaining native kidney was identified at a median follow-up of 56 months [31]. Recent reports showed that history of previous malignancy does not have an additive effect on CSS of transplant recipients who develop cancer [32]. Moreover, CSS and OS were reported as being comparable between patients with cancer recurrence after transplantation and patients who developed *de novo* cancers [33].

To summarize, KT is safe in patients with a history of SRM. The remaining native kidney should be followed-up, as there is an increased risk for RCC occurrence.

3.3. Post renal transplant SRM

Due to posttransplant immunosuppression, kidney transplant recipients are at an increased risk for developing malignancies [34], accounting as the third cause of mortality in

these patients, with calcineurin inhibitors being considered the most carcinogenic [35]. *De novo* renal tumors, either of the allograft, or the native kidney, are diagnosed in about 4.6% of kidney transplant recipients, with the latter being the most frequent site [36]. However, the majority of the diagnosed tumors are reported to be in early stage, low grade, and no significant difference in the mortality rate has been observed between KT patients with or without RCC [37]. On the other hand, graft survival seems to be decreased in patients with RCC, most probably due to back scaling of the immunosuppressive regimen [38].

In terms of prevention, several studies suggested that the administration of an immunosuppressive regimen containing mammalian target of rapamycin inhibitors (mTORis—sirolimus and everolimus) could reduce the occurrence of posttransplant SRM [39], due to their anti-tumoral effect particularly in RCC. However, a more recent study including 300 kidney transplant recipients who were randomized to receive cyclosporine or everolimus, showed a similar incidence of posttransplant malignancy in both groups [40].

3.3.1. Graft tumors

De novo renal tumors of the allograft kidney are rare findings, with an incidence below 0.5% [41]. Early diagnosis and nephron-sparing treatment are of utmost importance to preserve the renal function, to avoid the need of transplantectomy and return to dialysis. No specific factor has been associated with an increased risk of RCC in allograft kidneys [42].

The origin of the allograft tumors may be donor derived or recipient derived [43]. The time between transplantation and the diagnosis of an allograft tumor can range from 9 to 258 months or even more [44], but no association can be made between this period of time and tumor origin. In a recent report, Kijima et al. [45] presented the case of a male patient who received a kidney from a female living donor and developed an allograft tumor 14 years after transplantation. By using the fluorescence *in situ* hybridization technique, the authors showed that the tumor originated from the donor, whilst tumor vasculature originated from the recipient. On the other hand, *de novo* RCC of recipient originated from an allograft kidney has also been reported at 10 years after transplantation and it was attributed to the migration and homing of recipient-derived stem cells to the transplanted kidney, potentially secondary to tissue injury such as graft pyelonephritis [46].

Non-contrast enhanced computed tomography (CT) scan might easily miss the diagnosis [47], and as such, the recommended diagnostic protocol comprises abdominal ultrasound and contrast-enhanced CT or magnetic resonance imaging in case of any suspicion. Yearly, ultrasound is most commonly recommended to detect any new small mass in the allograft, allowing for a timely minimally-invasive treatment. The follow-up should be performed for indefinite time, as there have been reports of tumors diagnosed even in non-functioning grafts 29 years after KT [48].

Rarely, paraneoplastic syndromes, such as Guillain-Barre syndrome, can be associated with the presence of an allograft tumor. As such, in any suggestive context, paraneoplastic etiology should be excluded in all patients with a history of transplantation [49].

The most common histology of kidney allograft tumors is papillary RCC in up to 50% of cases, followed by clear cell carcinoma in about 33% of cases [50].

NSS of an allograft SRM is the standard treatment, but it is particularly difficult, as there can be local fibrosis and adherences to main renal blood vessels, significantly increasing the complexity of the surgery. Extraperitoneal access can be performed for tumors located on the convex edge, while the transperitoneal access is preferred for medially located tumors, allowing easier vascular control with possible hilar clamping [51]. In a multicenter analysis of 43 NSS for kidney allograft tumors, the oncologic safety of this approach has been proven, with no recurrences reported at a follow-up of 35.2 months. No graft loss has been reported and no patient returned to dialysis after surgery. The total rate of postoperative complications was 20.9%, of which 11.62% were of high grade [52].

Less invasive methods have been proposed in these patients as promising alternatives, such as radiofrequency ablation, cryoablation, microwave ablation, or high-intensity focused ultrasound [53]. The possibility to perform ablative therapy in local anesthesia, the low rate of complications, lack of need for vascular clamping, and minimal impact upon the renal function [54] make it suitable especially for elderly and frail patients. A recent systematic review showed that radiofrequency ablation was the most frequent treatment choice after NSS for allograft SRM, followed by cryosurgery. Complete tumor necrosis after ablative therapies can be proven by imaging and no differences in terms of efficiency have been identified between any of the ablative therapies. Among 100 procedures of ablative treatment in allograft kidneys, only three treatment failures were reported, with the possibility to repeat the ablative treatment [55]. No cancer-related deaths have been reported, but renal allograft loss has been identified in five cases. In another cohort of 20 patients who underwent local ablative therapy of allograft tumors, no recurrence was identified at a mean follow-up of 27.9 months [56].

No clear recommendations exist for the management of immunosuppressive therapy in patients with renal graft tumor for which NSS or ablative therapies are performed. In the majority of patients, the immunosuppression is maintained after minimally-invasive treatment of the graft SRM [45]. Tollefson et al. [57] showed a low rate of tumor progression in patients under efficient immunosuppression, demonstrating the safety of continuing this treatment in the perioperative setting for patients with localized disease. It is suggested that patients receiving azathioprine should be switched for mycophenolate mofetil, and cyclosporine could be switched for mammalian target of rapamycin inhibitors in order to avoid the effect on DNA synthesis (for azathioprine) or on transforming growth factor (for cyclosporine) [42], but evidence is still limited.

To conclude, yearly ultrasound performed after KT ensures the diagnosis of kidney allograft tumors in early stages, allowing for a nephron-sparing treatment and maximum preservation of the graft function.

3.3.2. Native kidney tumor

RCCs of the native kidney represent up to 5% of the malignancies diagnosed in kidney transplant recipients, with acquired cystic kidney disease and long-term dialysis being

the main risk factors [58]. Increased risk for developing RCC post-transplant was also reported among older patients, non-Caucasian recipients, patients with renal failure secondary to hypertension or glomerular disease, cyclosporine-based immunosuppression protocols, longer prednisone treatment, and current smokers [59,60]. In this context, bilateral or multifocal tumors are frequently diagnosed, as opposed to sporadic tumors [37]. Goh and Vathsala [61] proposed a screening schedule starting at 1 month after transplantation, followed by repeat ultrasound at 2 years for patients with cysts and at 5 years for patients without cysts. Other authors proposed yearly abdominal ultrasound to ensure an early diagnosis and favorable prognosis [62].

The time between KT and native nephrectomy for renal mass has been reported to be between 1 month and 14 years, with an average of 3 years [58]. Klatte and Marberger [63] suggested that a tumor can be considered as *de novo* if it has occurred at least 6 months after transplantation. The short interval to detection of RCC in some patients suggests that a proportion of these tumors were present before transplantation, as such pretransplant assessment should be improved. Imaging should be routinely performed in patients on renal transplant waiting list to avoid transplantation in case of advanced malignancy. The 2020 Kidney Disease Improving Global Outcomes (KDIGO) Clinical Practice guidelines recommend screening of renal transplant candidates specifically in high-risk setting: more than 3 years on dialysis, family history of RCC, acquired cystic disease, or analgesic nephropathy [64]. However, imaging performed immediately prior to the transplant might not always be possible, given that a significant proportion of kidney transplants come from deceased donors and not from planned procedures [65].

Clear cell and papillary RCC are the two most frequent histopathological types, but renal oncocytoma has been also reported in rare cases [66].

The diagnostic workup comprises abdominal ultrasound and contrast-enhanced CT. Contrast-enhanced ultrasound can be considered as a valuable imaging method, therefore, an alternative to CT to assess the morphology and vascularization of renal masses, with no risk of nephrotoxicity [67]. Moreover, contrast-enhanced ultrasound and magnetic resonance imaging might be superior for cystic mass classification [68].

The standard treatment of SRM is radical nephrectomy, given the incidence of multifocal tumors and the fact that native kidneys in transplant recipients are non-functional [69]. The laparoscopic approach is feasible, with low rate of perioperative complications. Recent reports showed that laparoscopic native nephrectomy and simultaneous living donor KT is a feasible approach in selected patients with suspicion SRMs [70].

Following curative surgery for localized disease, 5-year CSS rates are greater than 80% [63]. Similarly, Sultan et al. [70] reported no recurrences at 4 years follow-up in a group of 10 patients with pathologically confirmed RCC who underwent simultaneous native nephrectomy for SRM at the time of transplantation. However, Ryosaka et al. [71] observed that solid-type RCC of the native kidney diagnosed in KT patients has a significantly worse prognosis, with a lower rate of 5-year CSS and a higher recurrence rate as compared to patients without KT.

The general trend in a KT recipient with *de novo* malignancy was to perform back scaling of the immunosuppression regimen [38], which increases the risk of graft rejection. In this context, more recent reports showed that the immunosuppressive therapy can be continued safely in the perioperative period for patients with localized disease and timely resection [37]. Conversion of the immunosuppressive regimen to a proliferation signal inhibitor combination has been shown in preliminary studies to potentially improve patient survival in case of RCC [72], by inhibition of mTOR and the antiproliferative effects, but long-term results are awaited.

SRMs in native kidneys of transplant recipients are more frequently diagnosed in the context of acquired cystic disease or previous long-term dialysis. High-risk patients should be regularly followed-up by ultrasonography. Radical nephrectomy is the standard treatment with good postoperative prognosis.

4. Conclusion

The increasing demand of kidney grafts for patients with ESRD points out the need to expand the organ pool for KT. The use of graft with SRM may be considered a safe option after bench table tumor excision in both living and deceased donors. In case of a SRM detected in the graft after KT on periodic US-evaluation, NSS is the recommended treatment in order to preserve renal function. Ablative therapies can be considered in elderly and frail patients. In case of SMR finding in the native kidneys after KT, radical nephrectomy is recommended. Finally, immunosuppressive therapy can be safely administered despite the presence of SRM in either the native kidney or in the graft.

Author contributions

Protocol/project development: Alberto Piana, Angelo Territo, Alberto Breda.

Data collection: Alberto Piana, Iulia Andras, Riccardo Campi, Thomas Prudhomme, Vital Hevia, Roman Boissier.

Manuscript writing/editing: Alberto Piana, Iulia Andras, Angelo Territo, Pietro Diana, Paolo Verri, Andrea Gallioli.

Supervision: Angelo Territo, Alberto Piana.

Conflicts of interest

The authors declare no conflict of interest.

References

- [1] Johnson DW, Herzig K, Purdie D, Brown AM, Rigby RJ, Nicol DL, et al. A comparison of the effects of dialysis and renal transplantation on the survival of older uremic patients. *Transplantation* 2000;69:794–9.
- [2] Heldal K, Hartmann A, Grootendorst DC, de Jager DJ, Leivestad T, Foss A, et al. Benefit of kidney transplantation beyond 70 years of age. *Nephrol Dial Transplant* 2010;25:1680–7.
- [3] Ying T, Shi B, Kelly PJ, Pilmore H, Clayton PA, Chadban SJ. Death after kidney transplantation: an analysis by era

- and time post-transplant. *J Am Soc Nephrol* 2020;31:2887–99.
- [4] Ku E, McCulloch CE, Ahearn P, Grimes BA, Mitsnefes MM. Trends in cardiovascular mortality among a cohort of children and young adults starting dialysis in 1995 to 2015. *JAMA Netw Open* 2020;3:e2016197. <https://doi.org/10.1001/jamanetworkopen.2020.16197>.
 - [5] TNM classification of malignant tumours | UICC n.d. <https://www.uicc.org/resources/tnm>. [Accessed December 4, 2021].
 - [6] Wolfe RA, Ashby VB, Milford EL, Ojo AO, Ettenger RE, Agodoa LY, et al. Comparison of mortality in all patients on dialysis, patients on dialysis awaiting transplantation, and recipients of a first cadaveric transplant. *N Engl J Med* 1999;341:1725–30.
 - [7] Breda A, Territo A, Gausa L, Tuğcu V, Alcaraz A, Musquera M, et al. Robot-assisted kidney transplantation: the European experience. *Eur Urol* 2018;73:273–81.
 - [8] Musquera M, Peri L, Ajami T, Campi R, Tugcu V, Decaestecker K, et al. Robot-assisted kidney transplantation: update from the European Robotic Urology Section (ERUS) series. *BJU Int* 2021;127:222–8.
 - [9] Territo A, Piana A, Fontana M, Diana P, Gallioli A, Gaya JM, et al. Step-by-step development of a cold ischemia device for open and robotic-assisted renal transplantation. *Eur Urol* 2021;80:738–45.
 - [10] Au E, Wong G, Chapman JR. Cancer in kidney transplant recipients. *Nat Rev Nephrol* 2018;14:508–20.
 - [11] Leveridge M, Musquera M, Evans A, Cardella C, Pei Y, Jewett M, et al. Renal cell carcinoma in the native and allograft kidneys of renal transplant recipients. *J Urol* 2011;186:219–23.
 - [12] Breda A, Budde K, Figueiredo A, Lledó García E, Olsburgh J, Regele H. European Association of Urology Guidelines on Renal Transplantation 2022. <https://uroweb.org/guideline/renal-transplantation>. [Accessed 07 December 2021].
 - [13] Hollingsworth JM, Miller DC, Daignault S, Hollenbeck BK. Rising incidence of small renal masses: a need to reassess treatment effect. *J Natl Cancer Inst* 2006;98:1331–4.
 - [14] Escudier B, Porta C, Schmidinger M, Rioux-Leclercq N, Bex A, Khoo V, et al. Renal cell carcinoma: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Ann Oncol* 2019;30:706–20.
 - [15] Bianchi L, Schiavina R, Borghesi M, Chessa F, Casablanca C, Angiolini A, et al. Which patients with clinical localized renal mass would achieve the trifecta after partial nephrectomy? The impact of surgical technique. *Minerva Urol Nefrol* 2020;72:339–49.
 - [16] Umari P, Rizzo M, Billia M, Stacul F, Bertolotto M, Cova MA, et al. Oncological outcomes of active surveillance and percutaneous cryoablation of small renal masses are similar at intermediate term follow-up. *Minerva Urol Nephrol* 2022;74:321–8.
 - [17] Mershon JP, Tuong MN, Schenkman NS. Thermal ablation of the small renal mass: a critical analysis of current literature. *Minerva Urol Nefrol* 2020;72:123–34.
 - [18] Campi R, Sessa F, Corti F, Carrion DM, Mari A, Amparore D, et al. Triggers for delayed intervention in patients with small renal masses undergoing active surveillance: a systematic review. *Minerva Urol Nefrol* 2020;72:389–407.
 - [19] Bada M, Rapisarda S, Cicero C, Di Mauro M, Sebben M, DE Concilio B, et al. The role of renal biopsy to improve small renal mass diagnosis and management: are there predictive factors for a higher detection rate? The first Italian study of 100 cases. *Minerva Urol Nephrol* 2021;73:78–83.
 - [20] Stubenbord WT, Cheigh JS, Riggio RR. Kidney transplantation immediately following excision of a malignant tumor from the donor kidney: a case report with long-term follow-up. *Transplant Proc* 1982;14:775–6.
 - [21] Musquera M, Pérez M, Peri L, Esforzado N, Sebastià MC, Paredes D, et al. Kidneys from donors with incidental renal tumors: should they be considered acceptable option for transplantation? *Transplantation* 2013;95:1129–33.
 - [22] Hevia V, Hassan Zakri R, Fraser Taylor C, Bruins HM, Boissier R, Lledo E, et al. Effectiveness and harms of using kidneys with small renal tumors from deceased or living donors as a source of renal transplantation: a systematic review. *Eur Urol Focus* 2019;5:508–17.
 - [23] Sener A, Uberoi V, Bartlett ST, Kramer AC, Phelan MW. Living-donor renal transplantation of grafts with incidental renal masses after *ex-vivo* partial nephrectomy. *BJU Int* 2009;104:1655–60.
 - [24] Ogawa Y, Kojima K, Mannami R, Mannami M, Kitajima K, Nishi M, et al. Transplantation of restored kidneys from unrelated donors after resection of renal cell carcinoma: results from 10 patients. *Transplant Proc* 2015;47:1711–9.
 - [25] Brook NR, Gibbons N, Johnson DW, Nicol DL. Outcomes of transplants from patients with small renal tumours, live unrelated donors and dialysis wait-listed patients. *Transpl Int* 2010;23:476–83.
 - [26] Nicol DL, Preston JM, Wall DR, Griffin AD, Campbell SB, Isbel NM, et al. Kidneys from patients with small renal tumours: a novel source of kidneys for transplantation. *BJU Int* 2008;102:188–92. ; discussion 192–3.
 - [27] Livingston-Rosanoff D, Foley DP, Levenson G, Wilke LG. Impact of pre-transplant malignancy on outcomes after kidney transplantation: United Network for Organ Sharing database analysis. *J Am Coll Surg* 2019;229:568–79.
 - [28] Batabyal P, Chapman JR, Wong G, Craig JC, Tong A. Clinical practice guidelines on wait-listing for kidney transplantation: consistent and equitable? *Transplantation* 2012;94:703–13.
 - [29] Unterrainer C, Opelz G, Döhler B, Süsal C, Collaborative Transplant Study. Pretransplant cancer in kidney recipients in relation to recurrent and *de novo* cancer incidence post-transplantation and implications for graft and patient survival. *Transplantation* 2019;103:581–7.
 - [30] Acuna SA, Huang JW, Dossa F, Shah PS, Kim SJ, Baxter NN. Cancer recurrence after solid organ transplantation: a systematic review and meta-analysis. *Transplant Rev (Orlando)* 2017;31:240–8.
 - [31] Sheashaa HA, Rennke HG, Bakr MA, Abbas TM, Atta AF, Sangak A, et al. Impact of accidental discovery of renal cell carcinoma at time of renal transplantation on patient or graft survival. *Transplantation* 2011;92:1123–8.
 - [32] Viecelli AK, Lim WH, Macaskill P, Chapman JR, Craig JC, Clayton P, et al. Cancer-specific and all-cause mortality in kidney transplant recipients with and without previous cancer. *Transplantation* 2015;99:2586–92.
 - [33] Lim WH, Au E, Krishnan A, Wong G. Assessment of kidney transplant suitability for patients with prior cancers: is it time for a rethink? *Transpl Int* 2019;32:1223–40.
 - [34] Vajdic CM, McDonald SP, McCredie MRE, van Leeuwen MT, Stewart JH, Law M, et al. Cancer incidence before and after kidney transplantation. *JAMA* 2006;296:2823–31.
 - [35] Imao T, Ichimaru N, Takahara S, Kokado Y, Okumi M, Imamura R, et al. Risk factors for malignancy in Japanese renal transplant recipients. *Cancer* 2007;109:2109–15.
 - [36] Matevossian E, Novotny A, Vogelsang B, Mehler J, Stangl M, Thorban S, et al. Noninvasive therapy of incidental *de novo* renal cell carcinoma in a kidney allograft 12 years after transplantation: report of a case and review of literature. *Transplant Proc* 2008;40:915–7.
 - [37] Klatter T, Seitz C, Waldert M, de Martino M, Kikic Z, Böhmig GA, et al. Features and outcomes of renal cell carcinoma of native kidneys in renal transplant recipients. *BJU Int* 2010;105:1260–5.
 - [38] Machhi R, Mandelbrot DA, Al-Qaoud T, Astor BC, Parajuli S. Characteristics and graft survival of kidney transplant

- recipients with renal cell carcinoma. *Am J Nephrol* 2020;51:777–85.
- [39] Piselli P, Serraino D, Segoloni GP, Sandrini S, Piredda GB, Scolari MP, et al. Risk of *de novo* cancers after transplantation: results from a cohort of 7217 kidney transplant recipients, Italy 1997–2009. *Eur J Cancer* 2013;49:336–44.
- [40] Budde K, Lehner F, Sommerer C, Reinke P, Arns W, Eisenberger U, et al. Five-year outcomes in kidney transplant patients converted from cyclosporine to everolimus: the randomized ZEUS study. *Am J Transplant* 2015;15:119–28.
- [41] Barama A, St-Louis G, Nicolet V, Hadjeres R, Daloz P. Renal cell carcinoma in kidney allografts: a case series from a single center. *Am J Transplant* 2005;5:3015–8.
- [42] Ploussard G, Chambade D, Meria P, Gaudez F, Tariel E, Verine J, 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;109:195–9.
- [43] Morath C, Mueller M, Goldschmidt H, Schwenger V, Opelz G, Zeier M. Malignancy in renal transplantation. *J Am Soc Nephrol* 2004;15:1582–8.
- [44] Viart L, Surga N, Collon S, Jaureguy M, Elalouf V, Tillou X. The high rate of *de novo* graft carcinomas in renal transplant recipients. *Am J Nephrol* 2013;37:91–6.
- [45] Kijima Y, Iida S, Nozaki T, Sekido E, Toguchi M, Horiuchi T, et al. Fluorescence *in situ* hybridization for the origin of *de novo* renal cell carcinoma in a kidney allograft: a case report. *Transplant Proc* 2021;53:2552–5.
- [46] Verine J, Varna M, Ratajczak P, El-Bouchtaoui M, Leboeuf C, Plassa L-F, et al. Human *de novo* papillary renal-cell carcinomas in a kidney graft: evidence of recipient origin with adenoma-carcinoma sequence. *Am J Transplant* 2013;13:984–92.
- [47] Tillou X, Doerfler A, Collon S, Kleinclauss F, Patard J-J, Badet L, et al. *De novo* kidney graft tumors: results from a multicentric retrospective national study. *Am J Transplant* 2012;12:3308–15.
- [48] Akioka K, Masuda K, Harada S, Nakao T, Nakamura T, Okugawa K, et al. How long should we follow the post-transplantation patient after graft loss? A case report of renal cancer in the grafted kidney that occurred 16 years after graft loss. *Transplant Proc* 2014;46:626–9.
- [49] Zakrocka I, Baranowicz-Gąszczuk I, Korolczuk A, Zaluska W. Guillain-Barre syndrome: a typical paraneoplastic syndrome in a kidney transplant recipient with allograft renal cell carcinoma: a case report and review of the literature. *BMC Nephrol* 2020;21:434.
- [50] Troxell ML, Higgins JP. Renal cell carcinoma in kidney allografts: histologic types, including biphasic papillary carcinoma. *Hum Pathol* 2016;57:28–36.
- [51] Varotti G, Bertocchi M, Barabani C, Terulla A, Fontana I. Nephron-sparing surgery for malignancies in kidney allografts. *Transpl Int* 2015;28:1342–4.
- [52] Tillou X, Guleryuz K, Doerfler A, Bensadoun H, Chambade D, Codas R, et al. Nephron sparing surgery for *de novo* kidney graft tumor: results from a multicenter national study. *Am J Transplant* 2014;14:2120–5.
- [53] Tillou X, Guleryuz K, Collon S, Doerfler A. Renal cell carcinoma in functional renal graft: toward ablative treatments. *Transplant Rev (Orlando)* 2016;30:20–6.
- [54] de Gennaro F, Iezzi R, Spagnoletti G, Salerno MP, Romagnoli J, Citterio F. Image-guided thermal ablation in *de novo* renal tumor arising in kidney allograft: 3-year follow-up. A case report. *Transplant Proc* 2021;53:2539–42.
- [55] Favi E, Raison N, Ambrogi F, Delbue S, Clementi MC, Lamperti L, et al. Systematic review of ablative therapy for the treatment of renal allograft neoplasms. *World J Clin Cases* 2019;7:2487–504.
- [56] Cornelis F, Buy X, André M, Oyen R, Bouffard-Vercelli J, Blandino A, et al. *De novo* renal tumors arising in kidney transplants: midterm outcome after percutaneous thermal ablation. *Radiology* 2011;260:900–7.
- [57] Tollefson MK, Krambeck AE, Leibovich BC, Blute ML, Chow GK. Surgical treatment of renal cell carcinoma in the immunocompromised transplant patient. *Urology* 2010;75:1373–7.
- [58] Suson KD, Sausville JE, Sener A, Phelan MW. Native nephrectomy for renal cell carcinoma in transplant recipients. *Transplantation* 2011;91:1376–9.
- [59] Karami S, Yanik EL, Moore LE, Pfeiffer RM, Copeland G, Gonsalves L, et al. Risk of renal cell carcinoma among kidney transplant recipients in the United States. *Am J Transplant* 2016;16:3479–89.
- [60] Kleine-Döpke D, Oelke M, Schwarz A, Schwager Y, Lehner F, Klempnauer J, et al. Renal cell cancer after kidney transplantation. *Langenbecks Arch Surg* 2018;403:631–41.
- [61] 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.
- [62] Végső G, Toronyi E, Hajdu M, Piros L, Görög D, Deák PA, et al. Renal cell carcinoma of the native kidney: a frequent tumor after kidney transplantation with favorable prognosis in case of early diagnosis. *Transplant Proc* 2011;43:1261–3.
- [63] Klatte T, Marberger M. Renal cell carcinoma of native kidneys in renal transplant patients. *Curr Opin Urol* 2011;21:376–9.
- [64] Chadban SJ, Ahn C, Axelrod DA, Foster BJ, Kasiske BL, Kher V, et al. KDIGO Clinical Practice Guideline on the evaluation and management of candidates for kidney transplantation. *Transplantation* 2020;104:S11–103. <https://doi.org/10.1097/TP.0000000000003136>.
- [65] Moon A, Rogers A, Talbot D, Rix D. Renal cell cancer in a European regional renal transplant population: is there a role for immediate native renal radiological surveillance before and after transplantation? *Transplant Proc* 2015;47:1840–4.
- [66] Vernadakis S, Karaolani G, Moris D, Zavvos V, Liapis G, Zavos G. Multiple bilateral oncocytomas of the native kidneys following renal transplantation: report of a rare case and review of the literature. *World J Surg Oncol* 2013;11:119. <https://doi.org/10.1186/1477-7819-11-119>.
- [67] Villanueva LAA, Knust M, Quintella L, Suassuna JHR, Araújo NC. Renal oncocytoma in a kidney transplant patient: the imaging features on contrast-enhanced ultrasonography (CEUS): a case report. *J Bras Nefrol* 2018;40:86–90.
- [68] 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. <https://doi.org/10.1097/TP.0000000000003762>.
- [69] Shrewsbury AB, Osunkoya AO, Jiang K, Westby R, Canter D, Pattaras J, et al. Renal cell carcinoma in patients with end-stage renal disease has favorable overall prognosis. *Clin Transplant* 2014;28:211–6.
- [70] Sultan S, Finn C, Craig-Schapiro R, Aull M, Watkins A, Kapur S, et al. Simultaneous living donor kidney transplant and laparoscopic native nephrectomy: an approach to kidney transplant candidates with suspected renal-cell carcinoma. *J Endourol* 2021;35:1001–5.
- [71] Ryosaka M, Ishida H, Takagi T, Shimizu T, Tanabe K, Kondo T. Solid-type RCC originating from native kidneys in renal transplant recipients should be monitored cautiously. *Transpl Int* 2015;28:813–9.
- [72] Manuelli M, De Luca L, Iaria G, Tatangelo P, Sforza D, Perrone L, et al. Conversion to rapamycin immunosuppression for malignancy after kidney transplantation. *Transplant Proc* 2010;42:1314–6.