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**Treatment options for localised renal cell carcinoma of the transplanted kidney**

Motta G *et al*. Kidney allograft renal cell carcinoma

Gloria Motta, Mariano Ferraresso, Luca Lamperti, Dhanai Di Paolo, Nicholas Raison, Marta Perego, Evaldo Favi

**Gloria Motta,** Urology,IRCCS Policlinico San Donato, San Donato Milanese 27288, Italy

**Mariano Ferraresso, Luca Lamperti, Dhanai Di Paolo, Marta Perego, Evaldo Favi,**Renal Transplantation, Fondazione IRCCS Ca’ Granda Ospedale Maggiore Policlinico, Milan 20122, Italy

**Mariano Ferraresso, Evaldo Favi,** Department of Clinical Sciences and Community Health, University of Milan, Milan 20122, Italy

**Nicholas Raison,** MRC Centre for Transplantation, King’s College London, London WC2R 2LS, United Kingdom

**Author contributions:** Motta G contributed to literature review, data collection, data analysis, data interpretation, drafting the article, final approval; Ferraresso M, literature review, critical revision, and final approval; Lamperti L and Di Paolo D contributed to literature review, data collection, and final approval; Raison N contributed to drafting the article, language revision, and final approval; Perego M contributed to data collection, data analysis, editing the article, and final approval; Favi E contributed to literature review, data interpretation, drafting the article, critical revision, and final approval.

**Corresponding author: Evaldo Favi, MD, PhD, Senior Lecturer, Surgeon, Consultant** in Transplant and Vascular Access Surgery,Renal Transplantation, Fondazione IRCCS Ca’ Granda Ospedale Maggiore Policlinico, Via Francesco Sforza n. 28, Milan 20122, Italy. evaldofavi@gmail.com

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**Abstract**

Currently, there is no consensus among the transplant community about the treatment of renal cell carcinoma (RCC) of the transplanted kidney. Until recently, graftectomy was universally considered the golden standard, regardless of the characteristics of the neoplasm. Due to the encouraging results observed in native kidneys, conservative options such as nephron-sparing surgery (NSS) (enucleation and partial nephrectomy) and ablative therapy (radiofrequency ablation, cryoablation, microwave ablation, high-intensity focused ultrasound, and irreversible electroporation) have been progressively used in carefully selected recipients with early-stage allograft RCC. Available reports show excellent patient survival, optimal oncological outcome, and preserved renal function with acceptable complication rates. Nevertheless, the rarity and the heterogeneity of the disease, the number of options available, and the lack of long-term follow-up data do not allow to adequately define treatment-specific advantages and limitations. The role of active surveillance and immunosuppression management remain also debated. In order to offer a better insight into this difficult topic and to help clinicians choose the best therapy for their patients, we performed and extensive review of the literature. We focused on epidemiology, clinical presentation, diagnostic work up, staging strategies, tumour characteristics, treatment modalities, and follow-up protocols. Our research confirms that both NSS and focal ablation represent a valuable alternative to graftectomy for kidney transplant recipients with American Joint Committee on Cancer stage T1aN0M0 RCC. Data on T1bN0M0 lesions are scarce but suggest extra caution. Properly designed multi-centre prospective clinical trials are warranted.

**Key words:** Renal cell carcinoma; Kidney transplant; Graftectomy; Nephron-sparing surgery; Focal ablation; Review

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**Core tip:** Nephron-sparing surgery and ablative therapy have been increasingly recognised as a valuable alternative to transplantectomy in carefully selected kidney recipients with allograft renal cell carcinoma (RCC). The complexity of the disease, the numerosity of the treatments available, the lack of long-term follow-up data, and the relatively poor quality of the studies addressing this topic do not allow to properly define specific advantages and limitations of these conservative strategies. We performed an extensive review of the literature focusing on epidemiology, clinical presentation, diagnostic work up, staging strategies, tumour characteristics, treatment modalities, and follow-up protocols of localised RCC of the transplanted kidney.

**INTRODUCTION**

Kidney transplant (KTx) recipients have a survival advantage compared to patients on chronic dialysis or remaining on the transplant waiting list (TWL)[1,2]. Nevertheless, due to the synergistic effect of end-stage renal disease (ESRD) and prolonged exposure to powerful immunosuppressive agents, higher incidences of malignancies and inferior cancer-specific survivals than the general population have been reported[3-6]. Among neoplastic complications, renal cell carcinoma (RCC) of the transplanted kidney has been increasingly recognised as an important cause of morbidity and premature allograft loss[7-9]. Management can be exceptionally challenging because in this complex subset of patients the theoretical benefit of optimal oncological control must be carefully weighed against the substantial risk of death arising from technically demanding surgical procedures, peri-operative complications, and return to dialysis[8,10]. For many years, transplantectomy has been universally considered the golden standard, regardless of the characteristics of the lesion[11]. More recently, widespread and successful application of nephron-sparing surgery (NSS) and ablative therapy (AT) for the treatment of solid neoplasms in native kidneys[12] has favoured the use of conservative approaches in renal allografts[13]. Enucleation, partial nephrectomy (PN), radiofrequency ablation (RFA), cryoablation, microwave ablation (MWA), high-intensity focused ultrasound (HIFU), and irreversible electroporation (IRE) have been proposed as valuable alternatives to graftectomy in carefully selected recipients with localised RCC but evidence remain weak[13,14]. The rarity of the disease, the numerosity of the techniques, and the quality of the studies (mostly case reports or small retrospective case series) do not allow to adequately assess treatment-specific outcomes and to clearly define indications and limitations[13,14]. In particular, no clinical guidelines or comprehensive meta-analyses have been published and there is still concern in the transplant community regarding long-term efficacy and safety. In order to offer a better insight into this difficult topic and to help clinicians choose the best therapy for their patients, we performed and extensive review of the literature focusing on conservative treatments of localised RCC.

**Literature research**

PubMed was searched for manuscripts reporting on RCC of the transplanted kidney. No time limits were applied. The following key words combinations were used: “kidney transplant neoplasm”, “kidney transplant tumour”, “kidney transplant mass“, “kidney transplant cancer”, “kidney transplant renal cell carcinoma”, “renal transplant neoplasm”, “renal transplant tumour”, “renal transplant mass“, “renal transplant cancer”, “renal transplant renal cell carcinoma”, “kidney allograft neoplasm”, “kidney allograft tumour”, “kidney allograft mass“, “kidney allograft cancer”, “kidney allograft renal cell carcinoma”, “renal allograft neoplasm”, “renal allograft tumour”, “renal allograft mass“, “renal allograft cancer”, “renal allograft renal cell carcinoma”, “nephrectomy”, “transplantectomy”, “graftectomy”, “nephron-sparing surgery”, “ablation”, “radiofrequency ablation”, “cryoablation”, “microwave ablation”, “high-intensity focused ultrasound”, “irreversible electroporation”, “surveillance”, and “watchful waiting”. Preliminary screening was performed by Motta G, Ferraresso M, Lamperti L, Di Paolo D, and Favi E. Manuscripts reporting on localised kidney allograft RCC were further evaluated by Motta G and Favi E as a potential source of information for the review. Considered sub-topics were: epidemiology, clinical presentation, diagnosis, staging, neoplasms’ characteristics, treatment options, and follow-up strategies.

**EPIDEMIOLOGY**

Reported incidence of primary RCC in kidney allografts varies between 0.2% and 0.5%, depending on the series[7,15-18]. However, taking into account the progressive aging of the patients on the TWL[19], the increased utilization of expanded-criteria donors[20], and the significant amelioration of long-term recipient survival[2], it is reasonable to expect that the cumulative incidence of the disease will rise considerably in the next few years. KTx patients are approximately at 2-fold increased risk of developing malignancies than healthy controls[21]. Compared to the general population, the risk of developing RCC is 10-fold higher[22]. Even though, several studies have demonstrated an association between specific primary renal diseases, ESRD, long-term dialysis, immunosuppressive therapy and post-transplant RCC, the reason behind this increased susceptibility remains unknown[13,17,18,23,24]. Higher incidences of allograft RCC have been shown among patients receiving a kidney from a deceased donor compared to living donor recipients[7,13,14]. As pointed out by Griffith *et al*[7], this trend probably mirrors the disparity between the number of deceased and living donor transplants performed in most countries. Age differences and disparities in cancer screening protocols between donor types may also play a role[14,25]. Other possible variables such as deceased donor category, ethnicity, gender or age have not been extensively investigated. Regarding recipient’s characteristics, a disproportion of male patients with RCC of the transplanted kidney was observed by Tillou *et al*[13].

Allograft RCC are predominantly of donor origin[25]. However, lesions arising from recipient-derived cells have been reported[26]. Albeit generally neglected by current diagnostic and staging protocols, discriminating between transmitted and acquired allograft neoplasms might have relevant therapeutic and prognostic consequences that should encourage further investigation.

**CLINICAL PRESENTATION**

Overall, no more than 20% of the patients exhibit clinical manifestations of the disease[7]. The vast majority of lesions are asymptomatic and incidentally discovered during imaging studies performed as a part of the routine post-transplant follow-up or to rule out other conditions[7,13,14,18**,**27]. According to the largest studies available[7,13,14,18], most frequently reported symptoms eventually leading to the diagnosis of allograft RCC are haematuria, abdominal pain, asthenia, weight loss, fever, flu-like syndrome, hypertension, recurrent urinary tract infections, and allograft dysfunction.

**DIAGNOSIS**

Localised allograft RCC often represents an incidental finding[27]. Reported time intervals between transplantation and diagnosis are extremely variable[9,14,15,28]. Colour-Doppler ultrasound (US) is widely considered the first line modality for the evaluation of solid masses of the transplant[16,27,29]. In case of indeterminate lesions, contrast-enhanced computed tomography (CT) scan and magnetic resonance imaging (MRI) with or without contrast dye are the preferred options[14,18]. More recently, excellent results have been demonstrated using contrast-enhanced US (CEUS)[30]. Main advantages of CEUS over contrast-enhanced CT scan and MRI are lack of radiation exposure, avoidance of contrast-induced nephropathy (CIN) or nephrogenic systemic sclerosis, and cost savings[31]. In order to avoid diagnostic delays that may compromise the chance of conservative treatment or unnecessary interventions that may irreversibly damage the transplanted kidney, an allograft biopsy should be obtained whenever possible[7,14,18]. Histology not only allows to assess type, grading, and origin of the neoplasm but also provides fundamental information for epidemiological and clinical purposes.

**STAGING**

Since accepted indication for conservative treatment of allograft RCC is restricted to localised neoplasms, careful staging is mandatory. The staging system proposed by the American Joint Committee on Cancer (AJCC) for RCC in native kidneys is currently the most used tool in combination with the Fuhrman grading score[32,33]. However, the transplanted kidney has peculiar anatomical characteristics that may limit the use of standard staging tools. In this regard, the modified version of the AJCC staging system proposed by the Comité de Transplantation de l’Association Française d’Urologie seems a better option[18]. According to Tillou *et al*[18],T3 tumours extend into major veins or invade renal sinus fat or peritoneum whereas T4 lesions invade perinephric organs such as psoas muscle, iliac vessels wall, bladder, small intestine or colon. There is no consensus among the transplant community on the optimal staging work up. Contrast-enhanced abdomen CT scan and MRI with or without contrast material are the preferred imaging techniques in most centres[7,14,18,34].Albeit recommended by the American Urology Association (AUA) guidelines[32] and the European Association of Urology (EAU) guidelines[33], contrast-enhanced chest CT scan is seldom included in KTx RCC staging protocols.

**CANCER CHARACTERISTICS**

Similarly to native kidneys, three main variants of RCC have been identified in renal allografts: clear cell, papillary, and chromophobe[7,14,18]. Compared to the general population, a significantly higher prevalence of papillary type over clear cell type has been observed among KTx patients[7,14,18]. The reason behind this difference is obscure. Even though, papillary RCC is generally less aggressive than clear cell RCC, its multi-focality has been often considered a relative contraindication to conservative treatments[18,35-37]. More recently, results achieved with AT[14] have demonstrated that patients with papillary type RCC can be excellent candidate for allograft preservation strategies. Another interesting data is the high proportion of endophytic lesions successfully treated with AT[14]. Endophytic masses have been generally considered less suitable for AT than exophytic ones. The outcomes reported in renal allografts seem to contradict this opinion and suggest that tumour growth pattern may not be a relevant prognostic factor of primary treatment failure. According to the literature, the vast majority of localised allograft RCC successfully treated with NNS or AT is less than 4 cm in maximal diameter, Fuhrman grade 1-2, and staged T1aN0M0[14,18,34]. Conservative management of T1bN0M0 RCC remains anecdotal and seems to offer mixed outcomes[14,38-41].

**TREATMENT OPTIONS AND TREATMENT-SPECIFIC OUTCOMES**

***Graftectomy***

For many years, graftectomy has represented the only acceptable option for RCC of the transplanted kidney[14,42]. However, death rates as high as 3% with up to 50% of the patients experiencing severe post-operative complications have been reported following this aggressive surgical procedure[43]. Studies comparing NNS and AT to graftectomy, especially in recipients with T1aN0M0 lesions, have shown comparable oncological outcomes with fewer complications[7,14,42]. For these reasons, transplantectomy should be currently restricted to patients with irreversible allograft dysfunction, sarcomatoid type RCC, multi-focal papillary type RCC, RCC greater than 7 cm in maximal diameter (AJCC stage II), locally-invasive or metastatic RCC (AJCC stage III or IV), and RCC infiltrating critical structures. Recent data support this position and demonstrate that for T1aN0M0 RCC a 5-year survival rate of 95% can be expected[9,44] whereas 5-year survival rate after allograft removal and return to dialysis is only 34%[8]. Analyses of non-cancer specific mortality after KTx failure also confirm the long-term survival benefit of maintained renal function[45,46].

***NSS***

NSS techniques such as enucleation, wedge resection, and PN are now considered the treatment of choice for patients with T1aN0M0 RCC in native kidneys[32,33]. Albeit encouraging, experience in recipients with allograft RCC is limited[7,9,11,39,42,47]. Available studies demonstrate that with NSS excellent oncological outcomes can be obtained in patients with T1aN0M0 lesions. Local recurrence rates of less than 5%, lower post-operative complication rates (between 15% and 21%, depending on the series), marginal impact on allograft function, and the possibility to treat residual or relapsing neoplasms with further conservative strategies support NSS over transplantectomy. Successful resection of localised RCC greater than 4 cm in maximal diameter remains anecdotal and therefore should not favour the use of NSS over graftectomy[39,41]. Main limitations of NSS compared to AT are invasiveness, higher technical difficulty, and increased risk of peri-operative complications[7,14,18]. Most cases of NSS in transplant setting have been performed using an open technique but minimally invasive approaches have been also described[39,41]. The tumour can be resected getting access to the allograft *via* a retro- or an intra-peritoneal route depending on the location of the mass[39]. In case of lesions very close to the vessels, renal pedicle control is advised[39].

***RFA***

RFA is the preferred AT for KTx neoplasms (approximately, 80% of all the procedures reported in the literature)[14,48]. Excellent oncological and functional outcomes in the treatment of solid masses in native kidneys have undoubtedly favoured its application in the transplant setting[49-52]. RFA uses high-frequency alternating electrical current to force extra- and intra-cellular ions to follow the same route as the current thus generating agitation, frictional heat, and coagulative necrosis[53]. Relatively wide thermal dispersion and subsequent risk of thermal damage to critical peri-lesional structures represent the main limitations of the technique[53]. RFA has been mostly utilized to treat small exophytic lesions distant from the renal hilum[49,53]. However, experience in allograft RCC demonstrates that it can be effectively used for both exophytic and endophytic masses[14]. According to a recent systematic review[14], among 78 T1aN0M0 RCC treated with percutaneous US- or CT-guided RFA, only two episodes of primary treatment failure and one episode of local recurrence could be identified. Moreover, persistent and relapsing tumours were successfully managed by repeated ablation. Safety profile was also encouraging as no peri-operative deaths were recorded and complication rates did not exceed 15%. The most relevant adverse events were transient lower limb pain due to thermal injury to nerves or muscles and urinary leakage secondary to thermal damage to the renal pelvis. Renal function preservation was obtained in the vast majority of patients included in the analysis.

***Cryoablation***

Cryoablation uses a cryogenic freezing unit connected with special hollow needles to deliver a cooled fluid into the target-tissue and to simultaneously remove heat from it. At a cellular level, such a technique promotes ice crystal formation, irreversible membrane damage, cell lysis, and apoptosis whereas at a supra-cellular level, it causes ischemic necrosis secondary to intra-vascular coagulation[53]. Compared to RFA and MWA, cryoablation entails a lower risk of thermal damage to surrounding structures. For this reason, it is widely considered the most selective AT and it is particularly indicated for centrally located lesions[53]. Minimal impact on renal function represents another important feature[54]. Possible limitations, at least as shown in native kidneys, are higher risk of intra-operative bleeding[55], higher rate of primary treatment failure in case of neoplasms greater than 3 cm in maximal diameter[56-58], and higher recurrence rate for tumours with an endophytic growth pattern[59]. To date, only 10 cases of biopsy-proven T1aN0M0 and 1 case of biopsy-proven T1bN0M0 RCC of the transplanted kidney treated by cryoablation have been documented[34,60-63]. The procedures were mostly performed percutaneously under US- or CT-guidance with no persisting disease, no local relapse (post-ablation follow-up ranging from 1 to 59 mo), and excellent allograft function. Overall, there were 2 episodes of peri-operative bleeding[14].

***MWA***

MWA is a thermal ablation modality that uses microwaves to cause oscillation of polar molecules into the target-lesion thus generating frictional heat and coagulative necrosis[53]. Major advantages compared to other AT are the ability to deliver higher intra-lesion temperatures, a marginal dependency on tissue-specific electrical conductivity, simultaneous treatment of multiple neoplasms, and the possibility to ablate the puncture tract[53,64-66]. There are several studies supporting the application of MWA for malignant tumours in native kidneys[67,68] but experience in renal allografts is limited to a couple of small case series. Successful ablation of one Fuhrman grade 1-2, T1aN0M0 clear cell RCC and two Fuhrman grade 1-2, T1aN0M0 papillary RCC was first reported by Gul *et al*[63]. The procedures were performed under CT-guidance *via* a percutaneous or a trans-osseous approach with no serious complications, no allograft dysfunction, and no recurrence after a follow-up ranging from 8 to 61 mo. Other two cases of MWA of RCC of the transplanted kidney were more recently described by our group[69]. More in details, we treated one Fuhrman grade 2, T1aN0M0 papillary RCC and one Fuhrman grade 1, T1aN0M0 clear cell RCC. Ablations were carried out under US-guidance using an open retro-peritoneal route for the first patient and a percutaneous approach for the other one. Complete tumour destruction was achieved in both the operations without complications, loss of allograft function or recurrence after 3 and 5 years of follow-up, respectively.

***HIFU***

HIFU incorporates multiple US beams directed into a three-dimensional focal point to produce tissue destruction by combined effects of thermal and mechanical energies (more precisely, cavitation, micro-streaming, and radiation forces)[70]. Potential benefits of HIFU are fast action, minimal thermal dispersion, and reduced invasiveness as it does not require direct contact with the target-lesion[71,72]. On the contrary, recognised limitations of the technique are the need for an optimal acoustic window, the inability to reach deep organs or tissues due to US penetrance, and complex pre-operative planning[71,72]. Excellent results have been reported in native kidneys[73-75] but in KTx setting data are scarce. Searching the literature, we could find only three cases of allograft RCC treated by HIFU. US-guided percutaneous ablation of two T1aN0M0 papillary RCC was described by Di Candio *et al*[76] with excellent short-term oncological outcomes (6-mo follow-up) and no peri-operative adverse events whereas multiple unsuccessful attempts in a patient with a 55 mm T1bN0M0 clear cell RCC were reported by Chakera *et al*[77].

***IRE***

IRE is a non-thermal AT with extraordinary connective tissue-sparing properties that has been successfully used to treat renal[78] and extra-renal neoplasms[79]. This novel treatment modality utilizes an electrical field to generate nanopores into target-cells and induce permanent membrane permeability, disruption of homeostasis, and apoptosis[80,81]. It is particularly indicated in case of neoplastic lesions close to important vessels or structures. There is only one study describing the use of IRE in KTx tumours[63]. The procedure was performed percutaneously under CT-guidance to ablate a Fuhrman grade 3, T1aN0M0 clear cell RCC. The post-operative course was uneventful with preserved allograft function and no recurrence after 3 years of follow-up.

***Active surveillance***

There are no reports describing active surveillance (AS) in KTx recipients with RCC of the allograft. A major concern is that chronic immunosuppression may increase the risk of cancer spreading compared to the general population. Actually, such an assumption has never been confirmed. Recent studies have shown that growth rate and metastatic potential of transplant neoplasms are overall similar to those observed in native kidneys and in healthy controls[7,9,13,14,18,34]. As such, no hard recommendations can be made against the use of AS in the transplant setting. A reasonable approach would be to follow the principles stated by the AUA guidelines[32] and to consider both patient-related and tumour-related characteristics. As pointed out by Griffith *et al*[7], given the higher incidence of papillary RCC observed in recipients with allograft neoplasms[14,18,82], a lower threshold for renal mass biopsy is advised.

***Immunosuppression modification***

Immunosuppression is a well-recognised risk factor for the development of malignancies, particularly infectious-related ones and non-melanoma skin cancers (NMSC)[83]. Increased susceptibility to long-lasting viral infections with oncogenic potential and partial loss of immune-surveillance processes are considered the main reasons behind this phenomenon[21,84,85]. Associations between specific immunosuppressive drugs and risk of cancer after solid organ transplantation have been extensively investigated. Considering the role of NK[86], CD4+, and CD8+ T cells[87] in virus-specific immunity and in eliminating neoplastic cells, lymphocyte-depleting agents such as anti-thymocyte polyclonal antibodies[88] or anti-CD52 monoclonal antibody alemtuzumab[83,89] and calcineurin inhibitors (CNI) cyclosporine and tacrolimus[90] seem to play a major role. In particular, CNI have been shown to exert their action through indirect inhibition of T cells activation/proliferation (*via* decreased IL-2 production) and direct up-regulation of VEGF and TGF-b1[91,92]. A significant link between chronic azathioprine exposure and squamous cell carcinoma of the skin has been also demonstrated[93]. An accepted explanation is that azathioprine inhibits T cells proliferation and alters DNA repair mechanisms thus leading to impaired immune-surveillance and cell transformation. Data on cancer-related side effects of mycophenolic acid (MPA)[83,94,95] and results of the studies addressing the role of steroids in cancer development[83,87] remain unclear. There is mounting evidence that proliferation signal inhibitors (PSI)/mammalian target of rapamycin inhibitors (mTOR-I) sirolimus and everolimus may have important anti-neoplastic properties[83]. Main immunosuppressive action of mTOR-I is inhibition of T cells activation/proliferation through down-regulation of IL-2 and cell-cycle block. Nevertheless, the mTOR pathway regulates amino acid biosynthesis, glucose homeostasis, adipogenesis, actin cytoskeleton polarization, nutrient-response transcription programs, ribosome biosynthesis, size, growth, proliferation, aging, survival, and life-span of every human cell[96,97]. As such, mTOR signalling is also primarily involved in cancer growth, angiogenesis, and metastasis formation[96]. Outside the transplant setting, PSI have been successfully used for the treatment of neuro-endocrine tumours[98] and advanced RCC[99]. Encouraging results have been also obtained in KTx recipients with NMSC[100] and Kaposi’s sarcoma[101]. Currently, there are no formal recommendations on how to manage immunosuppression in patients with post-transplant malignancies but common trend is to reduce CNI and switch from MPA to mTOR-I whenever possible[83]. Recent reports suggest that using mTOR-I may be a valid option also in recipients with localised allograft RCC but larger populations and long-term outcomes are needed to confirm this hypothesis[7,9,13,18]. Increased risk of rejection[102] and severe drug-related side effects[103] are the main drawbacks of the strategy and therefore a tailored approach based on specific patient’s and cancer’s characteristics should be preferred.

**FOLLOW-UP STRATEGIES**

In our review, we found minimal information regarding follow-up protocols. Proposed strategies were also quite heterogeneous in terms of timing and techniques[7,14,18]. Overall, the risk of local recurrence and metastatic disease after successful treatment of T1aN0M0 and T1bN0M0 RCC in native kidneys is extremely low[32]. Albeit limited, experience in KTx suggests that cancer-specific outcomes are not significantly different[7,14,18,34]. As such, it seems reasonably safe to adopt what recommended by current AUA[32] or EAU guidelines[104]. Considering the risk and the burden of CIN in KTx recipients, colour-Doppler US, CEUS or MRI should be preferred over CT scan with contrast media[105]. After AT, discriminating between necrosis, inflammation, neoplastic tissue and normal parenchyma can be challenging[14]. In this context, protocol ablation-site biopsy may help promptly detect persistent or recurrent neoplasms[106].

**CONCLUSION**

Kidney allograft RCC represents a difficult challenge for the transplant community. Maximal renal function preservation is paramount to achieve the best outcome. In this regards, post-transplant routine follow-up colour-Doppler US may help detect lesions amenable of conservative treatment. Renal mass biopsy is advised for diagnostic purpose and proper treatment planning. Ideally, RCC should be assessed using the Fuhrman grading score and the modified AJCC staging system. Compared to the general population, higher incidences of papillary type RCC have been demonstrated among recipients with allograft neoplasms. Over years, improved surgical techniques and technological advances have favoured the use of NSS and AT over graftectomy. Available data on T1aN0M0 RCC are reassuring as they show excellent cancer-related outcomes, acceptable complication rates, and optimal allograft function whereas experience with T1bN0M0 remains mostly anecdotal (Table 1). RCC type and growth patter do not seem to affect primary treatment efficacy and relapse rates. Due to the rarity of the disease and the lack of properly designed studies, no hard recommendation can be made (Table 2). A reasonable approach would be to choose a tailored strategy considering both patient’s and tumour’s characteristics. Individual surgical risk and local expertise are also important. Multi-centre prospective comparative trials are warranted.

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**REFERENCES**

1 **Wolfe RA**, Ashby VB, Milford EL, Ojo AO, Ettenger RE, Agodoa LY, Held PJ, Port FK. 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**: 1725-1730 [PMID: 10580071 DOI: 10.1056/NEJM199912023412303]

2 **Favi E**, Salerno MP, Romagnoli J, Castagneto M, Citterio F. Significant improvement in patient survival after renal transplantation in the last decade. *Transplant Proc* 2011; **43**: 285-287 [PMID: 21335207 DOI: 10.1016/j.transproceed.2010.09.105]

3 **Birkeland SA**, Løkkegaard H, Storm HH. Cancer risk in patients on dialysis and after renal transplantation. *Lancet* 2000; **355**: 1886-1887 [PMID: 10866449 DOI: 10.1016/S0140-6736(00)02298-4]

4 **Mazzucotelli V**, Piselli P, Verdirosi D, Cimaglia C, Cancarini G, Serraino D, Sandrini S. De novo cancer in patients on dialysis and after renal transplantation: north-western Italy, 1997-2012. *J Nephrol* 2017; **30**: 851-857 [PMID: 28317077 DOI: 10.1007/s40620-017-0385-y]

5 **Taborelli M**, Toffolutti F, Del Zotto S, Clagnan E, Furian L, Piselli P, Citterio F, Zanier L, Boscutti G, Serraino D; Italian Transplant Cancer Cohort Study. Increased cancer risk in patients undergoing dialysis: a population-based cohort study in North-Eastern Italy. *BMC Nephrol* 2019; **20**: 107 [PMID: 30922296 DOI: 10.1186/s12882-019-1283-4]

6 **Au EH**, Chapman JR, Craig JC, Lim WH, Teixeira-Pinto A, Ullah S, McDonald S, Wong G. Overall and Site-Specific Cancer Mortality in Patients on Dialysis and after Kidney Transplant. *J Am Soc Nephrol* 2019; **30**: 471-480 [PMID: 30765426 DOI: 10.1681/ASN.2018090906]

7 **Griffith JJ**, Amin KA, Waingankar N, Lerner SM, Delaney V, Ames SA, Badani K, Palese MA, Mehrazin R. Solid Renal Masses in Transplanted Allograft Kidneys: A Closer Look at the Epidemiology and Management. *Am J Transplant* 2017; **17**: 2775-2781 [PMID: 28544435 DOI: 10.1111/ajt.14366]

8 **Rao PS**, Schaubel DE, Jia X, Li S, Port FK, Saran R. Survival on dialysis post-kidney transplant failure: results from the Scientific Registry of Transplant Recipients. *Am J Kidney Dis* 2007; **49**: 294-300 [PMID: 17261432 DOI: 10.1053/j.ajkd.2006.11.022]

9 **Diller R**, Senninger N. Treatment options and outcome for renal cell tumors in the transplanted kidney. *Int J Artif Organs* 2008; **31**: 867-874 [PMID: 19009504 DOI: 10.1177/039139880803101002]

10 **de'Angelis N**, Esposito F, Memeo R, Lizzi V, Martìnez-Pérez A, Landi F, Genova P, Catena F, Brunetti F, Azoulay D. Emergency abdominal surgery after solid organ transplantation: a systematic review. *World J Emerg Surg* 2016; **11**: 43 [PMID: 27582783 DOI: 10.1186/s13017-016-0101-6]

11 **Chambade D**, Meria P, Tariel E, Vérine J, De Kerviler E, Peraldi MN, Glotz D, Desgrandchamps F, Mongiat-Artus P. Nephron sparing surgery is a feasible and efficient treatment of T1a renal cell carcinoma in kidney transplant: a prospective series from a single center. *J Urol* 2008; **180**: 2106-2109 [PMID: 18804233 DOI: 10.1016/j.juro.2008.07.055]

12 **Van Poppel H**, Becker F, Cadeddu JA, Gill IS, Janetschek G, Jewett MA, Laguna MP, Marberger M, Montorsi F, Polascik TJ, Ukimura O, Zhu G. Treatment of localised renal cell carcinoma. *Eur Urol* 2011; **60**: 662-672 [PMID: 21726933 DOI: 10.1016/j.eururo.2011.06.040]

13 **Tillou X**, Guleryuz K, Collon S, Doerfler A. Renal cell carcinoma in functional renal graft: Toward ablative treatments. *Transplant Rev (Orlando)* 2016; **30**: 20-26 [PMID: 26318289 DOI: 10.1016/j.trre.2015.07.001]

14 **Favi E**, Raison N, Ambrogi F, Delbue S, Clementi MC, Lamperti L, Perego M, Bischeri M, Ferraresso M. Systematic review of ablative therapy for the treatment of renal allograft neoplasms. *World J Clin Cases* 2019; **7**: 2487-2504 [PMID: 31559284 DOI: 10.12998/wjcc.v7.i17.2487]

15 **Penn I**. Primary kidney tumors before and after renal transplantation. *Transplantation* 1995; **59**: 480-485 [PMID: 7878750 DOI: 10.1097/00007890-199559040-00006]

16 **Rouprêt M**, Peraldi MN, Thaunat O, Chrétien Y, Thiounn N, Dufour B, Kreis H, Méjean A. Renal cell carcinoma of the grafted kidney: how to improve screening and graft tracking. *Transplantation* 2004; **77**: 146-148 [PMID: 14724453 DOI: 10.1097/01.TP.0000097178.78160.F2]

17 **Buell JF**, Gross TG, Woodle ES. Malignancy after transplantation. *Transplantation* 2005; **80**: S254-S264 [PMID: 16251858 DOI: 10.1097/01.tp.0000186382.81130.ba]

18 **Tillou X**, Doerfler A, Collon S, Kleinclauss F, Patard JJ, Badet L, Barrou B, Audet M, Bensadoun H, Berthoux E, Bigot P, Boutin JM, Bouzguenda Y, Chambade D, Codas R, Dantal J, Deturmeny J, Devonec M, Dugardin F, Ferrière JM, Erauso A, Feuillu B, Gigante M, Guy L, Karam G, Lebret T, Neuzillet Y, Legendre C, Perez T, Rerolle JP, Salomon L, Sallusto F, Sénéchal C, Terrier N, Thuret R, Verhoest G, Petit J; “Comité de Transplantation de l’Association Française d’Urologie (CTAFU)”. De novo kidney graft tumors: results from a multicentric retrospective national study. *Am J Transplant* 2012; **12**: 3308-3315 [PMID: 22959020 DOI: 10.1111/j.1600-6143.2012.04248.x]

19 **Roodnat JI**, Zietse R, Mulder PG, Rischen-Vos J, van Gelder T, IJzermans JN, Weimar W. The vanishing importance of age in renal transplantation. *Transplantation* 1999; **67**: 576-580 [PMID: 10071030 DOI: 10.1097/00007890-199902270-00015]

20 **Pérez-Sáez MJ**, Montero N, Redondo-Pachón D, Crespo M, Pascual J. Strategies for an Expanded Use of Kidneys From Elderly Donors. *Transplantation* 2017; **101**: 727-745 [PMID: 28072755 DOI: 10.1097/TP.0000000000001635]

21 **Engels EA**, Pfeiffer RM, Fraumeni JF Jr, Kasiske BL, Israni AK, Snyder JJ, Wolfe RA, Goodrich NP, Bayakly AR, Clarke CA, Copeland G, Finch JL, Fleissner ML, Goodman MT, Kahn A, Koch L, Lynch CF, Madeleine MM, Pawlish K, Rao C, Williams MA, Castenson D, Curry M, Parsons R, Fant G, Lin M. Spectrum of cancer risk among US solid organ transplant recipients. *JAMA* 2011; **306**: 1891-1901 [PMID: 22045767 DOI: 10.1001/jama.2011.1592]

22 **Nepple KG**, Yang L, Grubb RL 3rd, Strope SA. Population based analysis of the increasing incidence of kidney cancer in the United States: evaluation of age specific trends from 1975 to 2006. *J Urol* 2012; **187**: 32-38 [PMID: 22088338 DOI: 10.1016/j.juro.2011.09.028]

23 **Chow WH**, Dong LM, Devesa SS. Epidemiology and risk factors for kidney cancer. *Nat Rev Urol* 2010; **7**: 245-257 [PMID: 20448658 DOI: 10.1038/nrurol.2010.46]

24 **Sassa N**, Hattori R, Tsuzuki T, Watarai Y, Fukatsu A, Katsuno S, Nishikimi T, Fujita T, Ohmae K, Gotoh M. Renal cell carcinomas in haemodialysis patients: does haemodialysis duration influence pathological cell types and prognosis? *Nephrol Dial Transplant* 2011; **26**: 1677-1682 [PMID: 20864552 DOI: 10.1093/ndt/gfq529]

25 **Desai R**, Collett D, Watson CJ, Johnson P, Evans T, Neuberger J. Cancer transmission from organ donors-unavoidable but low risk. *Transplantation* 2012; **94**: 1200-1207 [PMID: 23269448 DOI: 10.1097/TP.0b013e318272df41]

26 **Boix R**, Sanz C, Mora M, Quer A, Beyer K, Musulen E, González C, Bayona S, Saladié JM, Ariza A. Primary renal cell carcinoma in a transplanted kidney: genetic evidence of recipient origin. *Transplantation* 2009; **87**: 1057-1061 [PMID: 19352128 DOI: 10.1097/TP.0b013e31819d1e5f]

27 **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**: 91-96 [PMID: 23363786 DOI: 10.1159/000346624]

28 **Walton TJ**, McCulloch TA, Bishop MC. Aggressive renal cell carcinoma in a 27-year-old kidney transplant. *Nephrol Dial Transplant* 2005; **20**: 1018-1019 [PMID: 15769819 DOI: 10.1093/ndt/gfh748]

29 **Rodgers SK**, Sereni CP, Horrow MM. Ultrasonographic evaluation of the renal transplant. *Radiol Clin North Am* 2014; **52**: 1307-1324 [PMID: 25444108 DOI: 10.1016/j.rcl.2014.07.009]

30 **Harvey CJ**, Alsafi A, Kuzmich S, Ngo A, Papadopoulou I, Lakhani A, Berkowitz Y, Moser S, Sidhu PS, Cosgrove DO. Role of US Contrast Agents in the Assessment of Indeterminate Solid and Cystic Lesions in Native and Transplant Kidneys. *Radiographics* 2015; **35**: 1419-1430 [PMID: 26273994 DOI: 10.1148/rg.2015140222]

31 **Streb JW**, Tchelepi H, Malhi H, Deurdulian C, Grant EG. Retrospective Analysis of Contrast-enhanced Ultrasonography Effectiveness in Reducing Time to Diagnosis and Imaging-related Expenditures at a Single Large United States County Hospital. *Ultrasound Q* 2019; **35**: 99-102 [PMID: 30169489 DOI: 10.1097/RUQ.0000000000000375]

32 **Campbell S**, Uzzo RG, Allaf ME, Bass EB, Cadeddu JA, Chang A, Clark PE, Davis BJ, Derweesh IH, Giambarresi L, Gervais DA, Hu SL, Lane BR, Leibovich BC, Pierorazio PM. Renal Mass and Localized Renal Cancer: AUA Guideline. *J Urol* 2017; **198**: 520-529 [PMID: 28479239 DOI: 10.1016/j.juro.2017.04.100]

33 **Ljungberg B**, Albiges L, Abu-Ghanem Y, Bensalah K, Dabestani S, Fernández-Pello S, Giles RH, Hofmann F, Hora M, Kuczyk MA, Kuusk T, Lam TB, Marconi L, Merseburger AS, Powles T, Staehler M, Tahbaz R, Volpe A, Bex A. European Association of Urology Guidelines on Renal Cell Carcinoma: The 2019 Update. *Eur Urol* 2019; **75**: 799-810 [PMID: 30803729 DOI: 10.1016/j.eururo.2019.02.011]

34 **Guleryuz K**, Doerfler A, Codas R, Coffin G, Hubert J, Lechevallier E, Tillou X; Renal Transplantation Committee of the French Urological Association (CTAFU). A national study of kidney graft tumor treatments: Toward ablative therapy. *Surgery* 2016; **160**: 237-244 [PMID: 27032620 DOI: 10.1016/j.surg.2016.01.022]

35 **Roy C**, El Ghali S, Buy X, Lindner V, Gangi A. Papillary renal cell carcinoma in allograft kidney. *Eur Radiol* 2005; **15**: 661-665 [PMID: 15378336 DOI: 10.1007/s00330-004-2414-1]

36 **Delahunt B**, Eble JN. Papillary renal cell carcinoma: a clinicopathologic and immunohistochemical study of 105 tumors. *Mod Pathol* 1997; **10**: 537-544 [PMID: 9195569]

37 **Mejean A**, Hopirtean V, Bazin JP, Larousserie F, Benoit H, Chrétien Y, Thiounn N, Dufour B. Prognostic factors for the survival of patients with papillary renal cell carcinoma: meaning of histological typing and multifocality. *J Urol* 2003; **170**: 764-767 [PMID: 12913693 DOI: 10.1097/01.ju.0000081122.57148.ec]

38 **Vasisth G**, Kapoor A, Piercey K, Lambe S. Renal cell carcinoma in renal allograft: Case series and review of literature. *Urol Ann* 2018; **10**: 229-232 [PMID: 29719341 DOI: 10.4103/UA.UA\_66\_17]

39 **Varotti G**, Bertocchi M, Barabani C, Terulla A, Fontana I. Nephron-sparing surgery for malignancies in kidney allografts. *Transpl Int* 2015; **28**: 1342-1344 [PMID: 26190006 DOI: 10.1111/tri.12641]

40 **Tuzuner A**, Çakir F, Akyol C, Çelebi ZK, Ceylaner S, Ceylaner G, Sengül S, Keven K. Nephron-sparing surgery for renal cell carcinoma of the allograft after renal transplantation: report of two cases. *Transplant Proc* 2013; **45**: 958-960 [PMID: 23622598 DOI: 10.1016/j.transproceed.2013.02.054]

41 **Kaouk JH**, Spana G, Hillyer SP, White MA, Haber GP, Goldfarb D. Robotic-assisted laparoscopic partial nephrectomy for a 7-cm mass in a renal allograft. *Am J Transplant* 2011; **11**: 2242-2246 [PMID: 21827624 DOI: 10.1111/j.1600-6143.2011.03655.x]

42 **Tillou X**, Guleryuz K, Doerfler A, Bensadoun H, Chambade D, Codas R, Devonec M, Dugardin F, Erauso A, Hubert J, Karam G, Salomon L, Sénéchal C, Salusto F, Terrier N, Timsit MO, Thuret R, Verhoest G, Kleinclauss F; members of the Renal Transplantation Committee of the French Urological Association (CTAFU). Nephron sparing surgery for De Novo kidney graft tumor: results from a multicenter national study. *Am J Transplant* 2014; **14**: 2120-2125 [PMID: 24984974 DOI: 10.1111/ajt.12788]

43 **Chowaniec Y**, Luyckx F, Karam G, Glemain P, Dantal J, Rigaud J, Branchereau J. Transplant nephrectomy after graft failure: is it so risky? Impact on morbidity, mortality and alloimmunization. *Int Urol Nephrol* 2018; **50**: 1787-1793 [PMID: 30120679 DOI: 10.1007/s11255-018-1960-4]

44 **Zini L**, Patard JJ, Capitanio U, Crepel M, de La Taille A, Tostain J, Ficarra V, Bernhard JC, Ferrière JM, Pfister C, Villers A, Montorsi F, Karakiewicz PI. Cancer-specific and non-cancer-related mortality rates in European patients with T1a and T1b renal cell carcinoma. *BJU Int* 2009; **103**: 894-898 [PMID: 19076131 DOI: 10.1111/j.1464-410X.2008.08252.x]

45 **Brar A**, Markell M, Stefanov DG, Timpo E, Jindal RM, Nee R, Sumrani N, John D, Tedla F, Salifu MO. Mortality after Renal Allograft Failure and Return to Dialysis. *Am J Nephrol* 2017; **45**: 180-186 [PMID: 28110327 DOI: 10.1159/000455015]

46 **Gill JS**, Abichandani R, Kausz AT, Pereira BJ. Mortality after kidney transplant failure: the impact of non-immunologic factors. *Kidney Int* 2002; **62**: 1875-1883 [PMID: 12371992 DOI: 10.1046/j.1523-1755.2002.00640.x]

47 **Barama A**, St-Louis G, Nicolet V, Hadjeres R, Daloze P. Renal cell carcinoma in kidney allografts: a case series from a single center. *Am J Transplant* 2005; **5**: 3015-3018 [PMID: 16303018 DOI: 10.1111/j.1600-6143.2005.01099.x]

48 **Iezzi R**, Posa A, Romagnoli J, Salerno MP, Carchesio F, Veltri G, Spagnoletti G, Citterio F, Manfredi R. Radiofrequency thermal ablation of renal graft neoplasms: Case series and literature review. *Clin Transplant* 2018; **32**: e13432 [PMID: 30357920 DOI: 10.1111/ctr.13432]

49 **Lui KW**, Gervais DA, Arellano RA, Mueller PR. Radiofrequency ablation of renal cell carcinoma. *Clin Radiol* 2003; **58**: 905-913 [PMID: 14654022 DOI: 10.1016/S0009-9260(03)00222-8]

50 **Wagstaff P**, Ingels A, Zondervan P, de la Rosette JJ, Laguna MP. Thermal ablation in renal cell carcinoma management: a comprehensive review. *Curr Opin Urol* 2014; **24**: 474-482 [PMID: 25051022 DOI: 10.1097/MOU.0000000000000084]

51 **Prins FM**, Kerkmeijer LGW, Pronk AA, Vonken EPA, Meijer RP, Bex A, Barendrecht MM. Renal Cell Carcinoma: Alternative Nephron-Sparing Treatment Options for Small Renal Masses, a Systematic Review. *J Endourol* 2017; **31**: 963-975 [PMID: 28741377 DOI: 10.1089/end.2017.0382]

52 **Uhlig J**, Strauss A, Rücker G, Seif Amir Hosseini A, Lotz J, Trojan L, Kim HS, Uhlig A. Partial nephrectomy versus ablative techniques for small renal masses: a systematic review and network meta-analysis. *Eur Radiol* 2019; **29**: 1293-1307 [PMID: 30255245 DOI: 10.1007/s00330-018-5660-3]

53 **Hinshaw JL**, Lubner MG, Ziemlewicz TJ, Lee FT Jr, Brace CL. Percutaneous tumor ablation tools: microwave, radiofrequency, or cryoablation--what should you use and why? *Radiographics* 2014; **34**: 1344-1362 [PMID: 25208284 DOI: 10.1148/rg.345140054]

54 **Aron M**, Kamoi K, Remer E, Berger A, Desai M, Gill I. Laparoscopic renal cryoablation: 8-year, single surgeon outcomes. *J Urol* 2010; **183**: 889-895 [PMID: 20089263 DOI: 10.1016/j.juro.2009.11.041]

55 **Gervais DA**. Cryoablation versus radiofrequency ablation for renal tumor ablation: time to reassess? *J Vasc Interv Radiol* 2013; **24**: 1135-1138 [PMID: 23885912 DOI: 10.1016/j.jvir.2013.05.030]

56 **Finley DS**, Beck S, Box G, Chu W, Deane L, Vajgrt DJ, McDougall EM, Clayman RV. Percutaneous and laparoscopic cryoablation of small renal masses. *J Urol* 2008; **180**: 492-8; discussion 498 [PMID: 18550087 DOI: 10.1016/j.juro.2008.04.019]

57 **Laguna MP**, Beemster P, Kumar V, Klingler HC, Wyler S, Anderson C, Keeley FX, Bachmann A, Rioja J, Mamoulakis C, Marberger M, de la Rosette JJ. Perioperative morbidity of laparoscopic cryoablation of small renal masses with ultrathin probes: a European multicentre experience. *Eur Urol* 2009; **56**: 355-361 [PMID: 19467771 DOI: 10.1016/j.eururo.2009.05.002]

58 **Beemster PW**, Barwari K, Mamoulakis C, Wijkstra H, de la Rosette JJ, Laguna MP. Laparoscopic renal cryoablation using ultrathin 17-gauge cryoprobes: mid-term oncological and functional results. *BJU Int* 2011; **108**: 577-582 [PMID: 21044249 DOI: 10.1111/j.1464-410X.2010.09807.x]

59 **Tsivian M**, Lyne JC, Mayes JM, Mouraviev V, Kimura M, Polascik TJ. Tumor size and endophytic growth pattern affect recurrence rates after laparoscopic renal cryoablation. *Urology* 2010; **75**: 307-310 [PMID: 19942265 DOI: 10.1016/j.urology.2009.09.039]

60 **Shingleton WB**, Sewell PE. Percutaneous cryoablation of renal cell carcinoma in a transplanted kidney. *BJU Int* 2002; **90**: 137-138 [PMID: 12081786 DOI: 10.1046/j.1464-410X.2002.02761.x]

61 **Cornelis F**, Buy X, André M, Oyen R, Bouffard-Vercelli J, Blandino A, Auriol J, Correas JM, Pluvinage A, Freeman S, Solomon SB, Grenier N. De novo renal tumors arising in kidney transplants: midterm outcome after percutaneous thermal ablation. *Radiology* 2011; **260**: 900-907 [PMID: 21771957 DOI: 10.1148/radiol.11110122]

62 **Ploussard G**, Chambade D, Meria P, Gaudez F, Tariel E, Verine J, De Bazelaire C, Peraldi MN, Glotz D, Desgrandchamps F, Mongiat-Artus P. 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 [PMID: 21810160 DOI: 10.1111/j.1464-410X.2011.10315.x]

63 **Gul ZG**, Griffith JJ, Welch C, Fischman A, Palese MA, Badani KK, Mehrazin R. Focal Ablative Therapy for Renal Cell Carcinoma in Transplant Allograft Kidneys. *Urology* 2019; **125**: 118-122 [PMID: 30552936 DOI: 10.1016/j.urology.2018.12.003]

64 **Seror O**. Ablative therapies: Advantages and disadvantages of radiofrequency, cryotherapy, microwave and electroporation methods, or how to choose the right method for an individual patient? *Diagn Interv Imaging* 2015; **96**: 617-624 [PMID: 25981214 DOI: 10.1016/j.diii.2015.04.007]

65 **Cornelis FH**, Marcelin C, Bernhard JC. Microwave ablation of renal tumors: A narrative review of technical considerations and clinical results. *Diagn Interv Imaging* 2017; **98**: 287-297 [PMID: 28011104 DOI: 10.1016/j.diii.2016.12.002]

66 **Hernández JI**, Cepeda MF, Valdés F, Guerrero GD. Microwave ablation: state-of-the-art review. *Onco Targets Ther* 2015; **8**: 1627-1632 [PMID: 26185452 DOI: 10.2147/OTT.S81734]

67 **Choi SH**, Kim JW, Kim JH, Kim KW. Efficacy and Safety of Microwave Ablation for Malignant Renal Tumors: An Updated Systematic Review and Meta-Analysis of the Literature Since 2012. *Korean J Radiol* 2018; **19**: 938-949 [PMID: 30174484 DOI: 10.3348/kjr.2018.19.5.938]

68 **Shakeri S**, Afshari Mirak S, Mohammadian Bajgiran A, Pantuck A, Sisk A, Ahuja P, Lu DS, Raman SS. The effect of tumor size and location on efficacy and safety of US- and CT- guided percutaneous microwave ablation in renal cell carcinomas. *Abdom Radiol (NY)* 2019; **44**: 2308-2315 [PMID: 30847565 DOI: 10.1007/s00261-019-01967-8]

69 **Favi E**, Raiteri M, Paone G, Alfieri CM, Ferraresso M. Microwave Ablation of Renal Cell Carcinoma of the Transplanted Kidney: Two Cases. *Cardiovasc Intervent Radiol* 2019; **42**: 1653-1657 [PMID: 31388701 DOI: 10.1007/s00270-019-02302-w]

70 **She WH**, Cheung TT, Jenkins CR, Irwin MG. Clinical applications of high-intensity focused ultrasound. *Hong Kong Med J* 2016; **22**: 382-392 [PMID: 27380753 DOI: 10.12809/hkmj154755]

71 **Zhou YF**. High intensity focused ultrasound in clinical tumor ablation. *World J Clin Oncol* 2011; **2**: 8-27 [PMID: 21603311 DOI: 10.5306/wjco.v2.i1.8]

72 **Al-Bataineh O**, Jenne J, Huber P. Clinical and future applications of high intensity focused ultrasound in cancer. *Cancer Treat Rev* 2012; **38**: 346-353 [PMID: 21924838 DOI: 10.1016/j.ctrv.2011.08.004]

73 **Illing RO**, Kennedy JE, Wu F, ter Haar GR, Protheroe AS, Friend PJ, Gleeson FV, Cranston DW, Phillips RR, Middleton MR. The safety and feasibility of extracorporeal high-intensity focused ultrasound (HIFU) for the treatment of liver and kidney tumours in a Western population. *Br J Cancer* 2005; **93**: 890-895 [PMID: 16189519 DOI: 10.1038/sj.bjc.6602803]

74 **Ritchie RW**, Leslie T, Phillips R, Wu F, Illing R, ter Haar G, Protheroe A, Cranston D. Extracorporeal high intensity focused ultrasound for renal tumours: a 3-year follow-up. *BJU Int* 2010; **106**: 1004-1009 [PMID: 20230379 DOI: 10.1111/j.1464-410X.2010.09289.x]

75 **Wu F**, Wang ZB, Chen WZ, Bai J, Zhu H, Qiao TY. Preliminary experience using high intensity focused ultrasound for the treatment of patients with advanced stage renal malignancy. *J Urol* 2003; **170**: 2237-2240 [PMID: 14634387 DOI: 10.1097/01.ju.0000097123.34790.70]

76 **Di Candio G**, Porcelli F, Campatelli A, Guadagni S, Vistoli F, Morelli L. High-Intensity Focused Ultrasonography and Radiofrequency Ablation of Renal Cell Carcinoma Arisen in Transplanted Kidneys: Single-Center Experience With Long-Term Follow-Up and Review of Literature. *J Ultrasound Med* 2019; **38**: 2507-2513 [PMID: 30690771 DOI: 10.1002/jum.14938]

77 **Chakera A**, Leslie T, Roberts I, O'Callaghan CA, Cranston D. A lucky fall? Case report. *Transplant Proc* 2010; **42**: 3883-3886 [PMID: 21094877 DOI: 10.1016/j.transproceed.2010.08.031]

78 **Narayanan G**, Doshi MH. Irreversible Electroporation (IRE) in Renal Tumors. *Curr Urol Rep* 2016; **17**: 15 [PMID: 26769468 DOI: 10.1007/s11934-015-0571-1]

79 **Wu LM**, Zhang LL, Chen XH, Zheng SS. Is irreversible electroporation safe and effective in the treatment of hepatobiliary and pancreatic cancers? *Hepatobiliary Pancreat Dis Int* 2019; **18**: 117-124 [PMID: 30655073 DOI: 10.1016/j.hbpd.2019.01.001]

80 **Au JT**, Wong J, Mittra A, Carpenter S, Haddad D, Carson J, Jayaraman S, Monette S, Solomon SB, Ezell P, Fong Y. Irreversible electroporation is a surgical ablation technique that enhances gene transfer. *Surgery* 2011; **150**: 474-479 [PMID: 21878233 DOI: 10.1016/j.surg.2011.07.007]

81 **Thomson KR**, Cheung W, Ellis SJ, Federman D, Kavnoudias H, Loader-Oliver D, Roberts S, Evans P, Ball C, Haydon A. Investigation of the safety of irreversible electroporation in humans. *J Vasc Interv Radiol* 2011; **22**: 611-621 [PMID: 21439847 DOI: 10.1016/j.jvir.2010.12.014]

82 **Troxell ML**, Higgins JP. Renal cell carcinoma in kidney allografts: histologic types, including biphasic papillary carcinoma. *Hum Pathol* 2016; **57**: 28-36 [PMID: 27396934 DOI: 10.1016/j.humpath.2016.06.018]

83 **Krisl JC**, Doan VP. Chemotherapy and Transplantation: The Role of Immunosuppression in Malignancy and a Review of Antineoplastic Agents in Solid Organ Transplant Recipients. *Am J Transplant* 2017; **17**: 1974-1991 [PMID: 28394486 DOI: 10.1111/ajt.14238]

84 **Dantal J**, Soulillou JP. Immunosuppressive drugs and the risk of cancer after organ transplantation. *N Engl J Med* 2005; **352**: 1371-1373 [PMID: 15800234 DOI: 10.1056/NEJMe058018]

85 **Campistol JM**, Cuervas-Mons V, Manito N, Almenar L, Arias M, Casafont F, Del Castillo D, Crespo-Leiro MG, Delgado JF, Herrero JI, Jara P, Morales JM, Navarro M, Oppenheimer F, Prieto M, Pulpón LA, Rimola A, Román A, Serón D, Ussetti P; ATOS Working Group. New concepts and best practices for management of pre- and post-transplantation cancer. *Transplant Rev (Orlando)* 2012; **26**: 261-279 [PMID: 22902168 DOI: 10.1016/j.trre.2012.07.001]

86 **Morvan MG**, Lanier LL. NK cells and cancer: you can teach innate cells new tricks. *Nat Rev Cancer* 2016; **16**: 7-19 [PMID: 26694935 DOI: 10.1038/nrc.2015.5]

87 **Billups K**, Neal J, Salyer J. Immunosuppressant-driven de novo malignant neoplasms after solid-organ transplant. *Prog Transplant* 2015; **25**: 182-188 [PMID: 26107280 DOI: 10.7182/pit2015826]

88 **Wang K**, Xu X, Fan M. Induction therapy of basiliximab versus antithymocyte globulin in renal allograft: a systematic review and meta-analysis. *Clin Exp Nephrol* 2018; **22**: 684-693 [PMID: 28986715 DOI: 10.1007/s10157-017-1480-z]

89 **Hall EC**, Engels EA, Pfeiffer RM, Segev DL. Association of antibody induction immunosuppression with cancer after kidney transplantation. *Transplantation* 2015; **99**: 1051-1057 [PMID: 25340595 DOI: 10.1097/TP.0000000000000449]

90 **Crespo E**, Fernandez L, Lúcia M, Melilli E, Lauzurica R, Penin RM, Quer A, Luque S, Quero M, Manonelles A, Torras J, Cruzado JM, Cañas L, Grinyó JM, Bestard O. Effector Antitumor and Regulatory T Cell Responses Influence the Development of Nonmelanoma Skin Cancer in Kidney Transplant Patients. *Transplantation* 2017; **101**: 2102-2110 [PMID: 28403126 DOI: 10.1097/TP.0000000000001759]

91 **Maluccio M**, Sharma V, Lagman M, Vyas S, Yang H, Li B, Suthanthiran M. Tacrolimus enhances transforming growth factor-beta1 expression and promotes tumor progression. *Transplantation* 2003; **76**: 597-602 [PMID: 12923450 DOI: 10.1097/01.TP.0000081399.75231.3B]

92 **Engels EA**, Jennings L, Kemp TJ, Chaturvedi AK, Pinto LA, Pfeiffer RM, Trotter JF, Acker M, Onaca N, Klintmalm GB. Circulating TGF-β1 and VEGF and risk of cancer among liver transplant recipients. *Cancer Med* 2015; **4**: 1252-1257 [PMID: 25919050 DOI: 10.1002/cam4.455]

93 **Jiyad Z**, Olsen CM, Burke MT, Isbel NM, Green AC. Azathioprine and Risk of Skin Cancer in Organ Transplant Recipients: Systematic Review and Meta-Analysis. *Am J Transplant* 2016; **16**: 3490-3503 [PMID: 27163483 DOI: 10.1111/ajt.13863]

94 **Robson R**, Cecka JM, Opelz G, Budde M, Sacks S. Prospective registry-based observational cohort study of the long-term risk of malignancies in renal transplant patients treated with mycophenolate mofetil. *Am J Transplant* 2005; **5**: 2954-2960 [PMID: 16303010 DOI: 10.1111/j.1600-6143.2005.01125.x]

95 **Geissler EK**. Post-transplantation malignancies: here today, gone tomorrow? *Nat Rev Clin Oncol* 2015; **12**: 705-717 [PMID: 26483298 DOI: 10.1038/nrclinonc.2015.186]

96 **Pópulo H**, Lopes JM, Soares P. The mTOR signalling pathway in human cancer. *Int J Mol Sci* 2012; **13**: 1886-1918 [PMID: 22408430 DOI: 10.3390/ijms13021886]

97 **Moschetta M**, Reale A, Marasco C, Vacca A, Carratù MR. Therapeutic targeting of the mTOR-signalling pathway in cancer: benefits and limitations. *Br J Pharmacol* 2014; **171**: 3801-3813 [PMID: 24780124 DOI: 10.1111/bph.12749]

98 **Lamberti G**, Brighi N, Maggio I, Manuzzi L, Peterle C, Ambrosini V, Ricci C, Casadei R, Campana D. The Role of mTOR in Neuroendocrine Tumors: Future Cornerstone of a Winning Strategy? *Int J Mol Sci* 2018; **19**: [PMID: 29509701 DOI: 10.3390/ijms19030747]

99 **Ghidini M**, Petrelli F, Ghidini A, Tomasello G, Hahne JC, Passalacqua R, Barni S. Clinical development of mTor inhibitors for renal cancer. *Expert Opin Investig Drugs* 2017; **26**: 1229-1237 [PMID: 28952411 DOI: 10.1080/13543784.2017.1384813]

100 **Stucker F**, Marti HP, Hunger RE. Immunosuppressive drugs in organ transplant recipients--rationale for critical selection. *Curr Probl Dermatol* 2012; **43**: 36-48 [PMID: 22377918 DOI: 10.1159/000335148]

101 **Stallone G**, Schena A, Infante B, Di Paolo S, Loverre A, Maggio G, Ranieri E, Gesualdo L, Schena FP, Grandaliano G. Sirolimus for Kaposi's sarcoma in renal-transplant recipients. *N Engl J Med* 2005; **352**: 1317-1323 [PMID: 15800227 DOI: 10.1056/NEJMoa042831]

102 **Lim WH**, Eris J, Kanellis J, Pussell B, Wiid Z, Witcombe D, Russ GR. A systematic review of conversion from calcineurin inhibitor to mammalian target of rapamycin inhibitors for maintenance immunosuppression in kidney transplant recipients. *Am J Transplant* 2014; **14**: 2106-2119 [PMID: 25088685 DOI: 10.1111/ajt.12795]

103 **Nguyen LS**, Vautier M, Allenbach Y, Zahr N, Benveniste O, Funck-Brentano C, Salem JE. Sirolimus and mTOR Inhibitors: A Review of Side Effects and Specific Management in Solid Organ Transplantation. *Drug Saf* 2019; **42**: 813-825 [PMID: 30868436 DOI: 10.1007/s40264-019-00810-9]

104 **Donat SM**, Diaz M, Bishoff JT, Coleman JA, Dahm P, Derweesh IH, Herrell SD 3rd, Hilton S, Jonasch E, Lin DW, Reuter VE, Chang SS. Follow-up for Clinically Localized Renal Neoplasms: AUA Guideline. *J Urol* 2013; **190**: 407-416 [PMID: 23665399 DOI: 10.1016/j.juro.2013.04.121]

105 **Cheungpasitporn W**, Thongprayoon C, Mao MA, Mao SA, D'Costa MR, Kittanamongkolchai W, Kashani KB. Contrast-induced acute kidney injury in kidney transplant recipients: A systematic review and meta-analysis. *World J Transplant* 2017; **7**: 81-87 [PMID: 28280699 DOI: 10.5500/wjt.v7.i1.81]

106 **Aron M**, Hegarty NJ, Remer E, O'Malley C, Goldfarb D, Kaouk JH. Percutaneous radiofrequency ablation of tumor in transplanted kidney. *Urology* 2007; **69**: 778.e5-778.e7 [PMID: 17445675 DOI: 10.1016/j.urology.2007.01.090]

107 **Charboneau JW**, O'Loughlin MT, Milliner DS, Engen DE. Sonographically guided percutaneous radio frequency ablation of a renal cell carcinoma in a transplanted kidney. *J Ultrasound Med* 2002; **21**: 1299-1302 [PMID: 12418770 DOI: 10.7863/jum.2002.21.11.1299]

108 **Baughman SM**, Sexton WJ, Glanton CW, Dalrymple NC, Bishoff JT. Computerized tomography guided radio frequency ablation of a renal cell carcinoma within a renal allograft. *J Urol* 2004; **172**: 1262-1263 [PMID: 15371819 DOI: 10.1097/01.ju.0000140138.97968.ca]

109 **Goeman L**, Joniau S, Oyen R, Van Poppel H. Percutaneous ultrasound-guided radiofrequency ablation of recurrent renal cell carcinoma in renal allograft after partial nephrectomy. *Urology* 2006; **67**: 199 [PMID: 16413367 DOI: 10.1016/j.urology.2005.07.039]

110 **Matevossian E**, Novotny A, Vogelsang B, Mehler J, Stangl M, Thorban S, Dobritz M. 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**: 915-917 [PMID: 18555077 DOI: 10.1016/j.transproceed.2008.03.042]

111 **Veltri A**, Grosso M, Castagneri F, Garetto I, Sacchetto P, Tosetti I, Stratta P, Terrone C, Fava C. Radiofrequency thermal ablation of small tumors in transplanted kidneys: an evolving nephron-sparing option. *J Vasc Interv Radiol* 2009; **20**: 674-679 [PMID: 19299170 DOI: 10.1016/j.jvir.2009.01.018]

112 **Sanchez K**, Barr RG. Contrast-enhanced ultrasound detection and treatment guidance in a renal transplant patient with renal cell carcinoma. *Ultrasound Q* 2009; **25**: 171-173 [PMID: 19956049 DOI: 10.1097/RUQ.0b013e3181b4f9cf]

113 **Elkentaoui H**, Robert G, Pasticier G, Bernhard JC, Couzi L, Merville P, Ravaud A, Ballanger P, Ferrière JM, Wallerand H. Therapeutic management of de novo urological malignancy in renal transplant recipients: the experience of the French Department of Urology and Kidney Transplantation from Bordeaux. *Urology* 2010; **75**: 126-132 [PMID: 19864001 DOI: 10.1016/j.urology.2009.06.106]

114 **Olivani A**, Iaria M, Missale G, Capocasale E, Biasini E, Mazzoni MP, Lombardelli L, Luzi E, Frattini A, Pelosi G. Percutaneous ultrasound-guided radiofrequency ablation of an allograft renal cell carcinoma: a case report. *Transplant Proc* 2011; **43**: 3997-3999 [PMID: 22172886 DOI: 10.1016/j.transproceed.2011.08.089]

115 **Leveridge M**, Musquera M, Evans A, Cardella C, Pei Y, Jewett M, Robinette M, Finelli A. Renal cell carcinoma in the native and allograft kidneys of renal transplant recipients. *J Urol* 2011; **186**: 219-223 [PMID: 21575970 DOI: 10.1016/j.juro.2011.03.032]

116 **Swords DC**, Al-Geizawi SM, Farney AC, Rogers J, Burkart JM, Assimos DG, Stratta RJ. Treatment options for renal cell carcinoma in renal allografts: a case series from a single institution. *Clin Transplant* 2013; **27**: E199-E205 [PMID: 23419131 DOI: 10.1111/ctr.12088]

117 **Végső G**, Toronyi É, Deák PÁ, Doros A, Langer RM. Detection and management of renal cell carcinoma in the renal allograft. *Int Urol Nephrol* 2013; **45**: 93-98 [PMID: 22941752 DOI: 10.1007/s11255-012-0274-1]

118 **Su MZ**, Campbell NA, Lau HM. Management of renal masses in transplant allografts at an Australian kidney-pancreas transplant unit. *Transplantation* 2014; **97**: 654-659 [PMID: 24212503 DOI: 10.1097/01.TP.0000437333.38786.fd]

119 **Christensen SF**, Hansen JM. Donor Kidney With Renal Cell Carcinoma Successfully Treated With Radiofrequency Ablation: A Case Report. *Transplant Proc* 2015; **47**: 3031-3033 [PMID: 26707334 DOI: 10.1016/j.transproceed.2015.10.039]

120 **Hernández-Socorro CR**, Henríquez-Palop F, Santana-Toledo L, Gallego-Samper R, Rodríguez-Pérez JC. Radiofrequency ablation as an alternative therapy for renal neoplasms in graft recipients. A preliminary study. *Nefrologia* 2015; **35**: 514-516 [PMID: 26306951 DOI: 10.1016/j.nefro.2015.03.005]

121 **Cool DW**, Kachura JR. Radiofrequency Ablation of T1a Renal Cell Carcinomas within Renal Transplant Allografts: Oncologic Outcomes and Graft Viability. *J Vasc Interv Radiol* 2017; **28**: 1658-1663 [PMID: 28916346 DOI: 10.1016/j.jvir.2017.07.023]

122 **Mundel TM**, Schaefer KL, Colombo-Benkmann M, Dietl KH, Diallo-Danebrock R, Senninger N. Nephron-sparing surgery of a low grade renal cell carcinoma in a renal allograft 12 years after transplantation. *Cancer Biol Ther* 2007; **6**: 1700-1703 [PMID: 17986871 DOI: 10.4161/cbt.6.11.5165]

123 **Ribal MJ**, Rodriguez F, Musquera M, Segarra J, Guirado L, Villavicencio H, Alcaraz A. Nephron-sparing surgery for renal tumor: a choice of treatment in an allograft kidney. *Transplant Proc* 2006; **38**: 1359-1362 [PMID: 16797303 DOI: 10.1016/j.transproceed.2006.03.033]

124 **Lamb GW**, Baxter GM, Rodger RS, Aitchison M. Partial nephrectomy used to treat renal cell carcinoma arising in a live donor transplant kidney. *Urol Res* 2004; **32**: 89-92 [PMID: 15250100 DOI: 10.1007/s00240-003-0380-8]

**Footnotes**

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**Table 1 Summary of conservative treatments of localised allograft renal cell carcinoma1**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **RFA** | **CA** | **MWA** | **HIFU** | **IRE** | **NSS** |
| Ref. | Charboneau *et al*[107] | Shingleton *et al*[60] | Gul *et al*[63] | Chakera *et al*[77] | Gul[63] | Chambade *et al*[11] |
|  | Baughman *et al*[108] | Cornelis *et al*[61] | Favi *et al*[69] | Di Candio *et al*[76] |  | Varotti *et al*[39] |
|  | Roy *et al*[35] | Ploussard *et al*[62] |  |  |  | Tillou *et al*[42] |
|  | Goeman *et al*[109] | Guleryuz *et al*[34] |  |  |  | Barama *et al*[47] |
|  | Aron *et al*[106] | Gul *et al*[63] |  |  |  | Kaouk *et al*[41] |
|  | Matevossian *et al*[110] |  |  |  |  | Mundel *et al*[122] |
|  | Veltri *et al*[111] |  |  |  |  | Ribal *et al*[123] |
|  | Sanchez *et al*[112] |  |  |  |  | Lamb *et al*[124] |
|  | Elkentaoui *et al*[113] |  |  |  |  |  |
|  | Olivani *et al*[114] |  |  |  |  |  |
|  | Cornelis *et al*[61] |  |  |  |  |  |
|  | Leveridge *et al*[115] |  |  |  |  |  |
|  | Tillou *et al*[18] |  |  |  |  |  |
|  | Swords *et al*[116] |  |  |  |  |  |
|  | Végső *et al*[117] |  |  |  |  |  |
|  | Su *et al*[118] |  |  |  |  |  |
|  | Christensen *et al*[119] |  |  |  |  |  |
|  | Hernández-Socorro *et al*[120] |  |  |  |  |  |
|  | Guleryuz *et al*[34] |  |  |  |  |  |
|  | Cool *et al*[121] |  |  |  |  |  |
|  | Iezzi *et al*[48] |  |  |  |  |  |
|  | Di Candio *et al*[76] |  |  |  |  |  |
| Patients (*n*) | 70 | 11 | 5 | 3 | 1 | 61 |
| Lesions (*n*) | 78 | 11 | 5 | 3 | 1 | 63 |
| FU (range) | 3-71 mo | 1-59 mo | 8-61 mo | 73-81 mo | 34 mo | 5-109 mo |
| RCC type |  |  |  |  |  |  |
|  CC (*n*) | 10 | 7 | 2 | 1 | 1 | 24 |
|  PA (*n*) | 41 | 3 | 3 | 2 | 0 | 33 |
|  Other (*n*) | 5 | 1 | 0 | 0 | 0 | 2 |
|  NA (*n*) | 22 | 0 | 0 | 0 | 0 | 4 |
| Size (range) | 0.5-4.0 cm | 1-4.1 cm | 2.2-3.1 cm | 0.8-5.5 cm | 1.6 cm | 0.9-7.0 cm |
| TNM2 |  |  |  |  |  |  |
|  T1aN0M0 (*n*) | 78 | 10 | 5 | 2 | 1 | 60 |
| T1bN0M0 (*n*) | 0 | 1 | 0 | 1 | 0 | 3 |
| PTF (*n*) | 2 | 0 | 0 | 1 | 0 | 0 |
| Relapse (*n*) | 1 | 0 | 0 | 0 | 0 | 0 |
| DSM (*n*) | 0 | 0 | 0 | 0 | 0 | 0 |
| 1Summaries based on individual cases should not considered as an estimate of the “real world”. 2American Joint Committee on Cancer Tumour Node Metastasis Staging System. RFA: Radiofrequency ablation; CA: Cryoablation; MWA: Microwave ablation; HIFU: High-intensity focused ultrasound; IRE: Irreversible electroporation; NSS: Nephron-sparing surgery; FU: Follow-up; RCC: Renal cell carcinoma; CC: Clear cell; PA: Papillary; NA: Not available; TNM: Tumour node metastasis; PTF: Primary treatment failure; DSM: Disease-specific mortality. |

**Table 2 Advantages and limitations of conservative treatments of localised allograft renal cell carcinoma**

|  |  |  |
| --- | --- | --- |
|  | **Advantages** | **Limitations** |
| Nephron-sparing surgery | Complete tumour removal. | Technically demanding. |
|  | Definitive histology. | Invasive. |
|  | Easy imaging-based follow-up. | Higher peri-operative complication rate. |
|  | Good preliminary results with T1bN0M0. | Higher risk of allograft dysfunction. |
| Focal ablation | Minimally invasive. | Higher risk of primary treatment failure. |
|  | Highly selective. | Lack of definitive histology. |
|  | Can treat centrally located lesions. | Difficult imaging-based follow-up. |
|  | Lower peri-operative complication rate. | Dubious results with T1bN0M0. |
|  | Better allograft function preservation. |  |