EJT European Journal of Transplantation

2024;2:73-76
DOI: 10.57603/EJT-1836

KIDNEY TRANSPLANTATION IN PATIENTS WITH PREVIOUS RENAL CANCER

Alessandra Panarese[1,2], Lucia Romano[2], Laura Lancione[2], Antonio Giuliani[1,2], Tarek Hassan[1,2], Elisabetta Iacobelli[1,2], Marco Clementi[1,2], Martina Padula[1,2], Irene Tucceri Cimini[1,2], Fabio Vistoli[1,2]

[1] Department of Biotechnological and Applied Clinical Sciences (DISCAB), University of L'Aquila, L'Aquila, Italy; [2] Department of General and Transplant Surgery, San Salvatore Hospital, ASL1 Abruzzo, Coppito, L'Aquila, Italy

Summary

Background. The incidence of renal cell carcinoma (RCC) is significantly elevated in patients with end-stage renal disease (ESRD). With advancements in imaging, incidental discovery of small renal masses during pre-transplant evaluation is common. While a history of RCC was historically an absolute contraindication to transplantation, modern evidence advocates for a nuanced, risk-adapted approach

Methods. We conducted a narrative review synthesizing evidence from recent registry analyses, cohort studies, and clinical guidelines to evaluate the oncologic safety of kidney transplantation, graft outcomes, and optimal surveillance strategies in recipients with a prior history of RCC.

Discussion. For localized, low-grade RCC (≤ T1a) completely excised with negative margins, the recurrence risk is minimal, permitting immediate or early listing for transplantation without a mandatory waiting period. For larger or higher-grade tumors, individualized waiting periods (2-5 years) based on tumor stage and histology remain prudent. The surgical approach should be tailored to native renal function, with radical nephrectomy preferred in dialysis-dependent patients and nephron-sparing surgery for those with preserved function. Post-transplant immunosuppression regimens should consider mTOR inhibitors for their potential antineoplastic benefits. Lifelong, risk-stratified imaging surveillance is paramount for early detection of recurrence.

Conclusions. Kidney transplantation following curative treatment of small, localized RCC is oncologically safe and should not be unnecessarily delayed. A multidisciplinary, risk-adapted management strategy that includes personalized surveillance and immunosuppression protocols optimizes both patient and graft outcomes.

Key words: renal cell carcinoma, kidney transplantation, immunosuppression, cancer recurrence, oncologic risk, waitlisting

Received: November 22, 2025
Accepted: November 24, 2025

Correspondence
Lucia Romano
E-mail: lucia.romano@guest.graduate.univaq.it

How to cite this article: Panarese A, Romano L, Lancione L, et al. Kidney transplantation in patients with previous renal cancer. EJT 2025;3:73-76. https://doi.org/10.57603/EJT-1836

INTRODUCTION

Renal cell carcinoma (RCC) constitutes approximately 2-3% of all adult malignancies globally, with an estimated 400,000 new cases diagnosed annually [1,2]. Patients with end-stage renal disease (ESRD) face a substantially amplified risk of developing RCC, estimated to be 3-5 times higher than that of the general

population [3,4]. This elevated risk is attributed to the uremic state, characterized by chronic inflammation, oxidative stress, and immune dysregulation. Consequently, with aging dialysis populations and prolonged exposure to renal replacement therapy, transplant clinicians are increasingly confronted with candidates who have a history of, or present with, incidentally detected RCC.

Historically, any prior diagnosis of RCC was considered a contraindication to kidney transplantation, mandating prolonged, often arbitrary, cancer-free waiting periods. This conservative stance was rooted in concerns that post-transplant immunosuppression would precipitate cancer recurrence. However, accumulating evidence from large registry studies and cohort analyses has fundamentally challenged this dogma. It is now recognized that for patients with localized, low-grade, and completely resected tumors, the risk of post-transplant recurrence is negligible. Therefore, subjecting these individuals to prolonged dialysis may confer unnecessary morbidity and mortality without meaningful oncologic benefit [5,6]. This manuscript reviews the contemporary evidence guiding the evaluation, management, and post-transplant care of kidney transplant candidates with a history of RCC, advocating for a risk-stratified approach.

MATERIALS AND METHODS

In July 2025, we performed a narrative literature synthesis to summarize the current state of evidence. A search of PubMed, Embase, and the Cochrane Library was conducted for relevant English-language publications from the past decade (2014-2025). Search terms included combinations of "Kidney Transplantation", "Renal Transplantation", "Renal Cell Carcinoma", "Kidney Cancer", and "Pretransplant Malignancy". The reference lists of retrieved articles were also manually screened for additional relevant publications.

We prioritized full-text journal articles, including registry analyses, cohort studies (both prospective and retrospective), and clinical practice guidelines. Case reports, letters, editorials, and abstracts were excluded. Studies focusing solely on *de novo* RCC arising after transplantation were also excluded. A PRISMA flow chart [7] of the search strategy is shown in Figure 1.

The identified literature was analyzed to extract data on key themes: (1) oncologic outcomes and recurrence risk post-transplantation; (2) recommendations for waitlisting and optimal waiting periods; (3) surgical management strategies in potential transplant candidates; (4) the role of immunosuppression; and (5) post-transplant surveillance protocols. A narrative synthesis of these findings was constructed to provide a comprehensive overview for clinicians.

Full-text articles complying with the inclusion criteria were screened, and the following information was entered into a structured Excel data table: study characteristics (i.e. the first author's last name, year of publication, country of participating institution, type of study) (Tab. I).

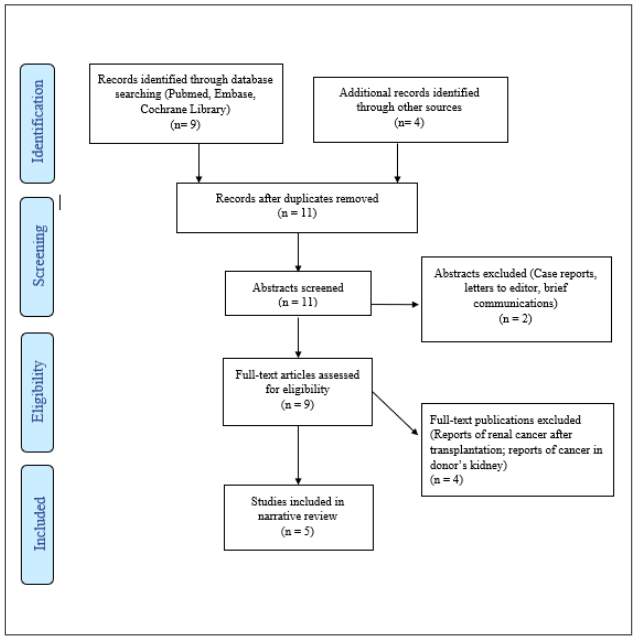

Figure 1. PRISMA 2009 flow diagram.

RESULTS

Epidemiology and unique tumor biology in ESRD

The global incidence of RCC shows significant geographical variation, with rates typically ranging from 13-17 and 7-10 per 100,000 in men and women, respectively [2]. The risk escalates dramatically in the ESRD population, particularly among individuals with dialysis durations exceeding ten years [3,4]. Importantly, RCC arising in the context of ESRD often exhibits distinct histopathological features, with a higher prevalence of papillary and acquired cystic disease-associated subtypes, which are frequently multifocal and demonstrate a more indolent biological

Table I. Characteristics of the included studies.

Author	Year	Country	Type of study
Dahle, Skauby [5]	2021	Norway	Review
Frascà, Brigante [6]	2018	Italy	Review
Boissier, Hevia [7]	2018	France	Review
Pascual, Abramowicz [8]	2014	Spain	Clinical practice guideline
Cognard, Anglicheau [9]	2017	France	Retrospective

behavior compared to sporadic clear cell RCC [11]. This difference in tumor biology is a cornerstone of the revised, more permissive approach to transplantation.

Surgical management: balancing oncology and nephrology

The surgical approach to RCC in a potential transplant candidate must be meticulously planned, balancing oncologic radicality with the preservation of renal function:

- Radical nephrectomy: for patients already dependent on dialysis, radical nephrectomy is the procedure of choice. In this context, preserving non-functioning renal parenchyma offers no clinical benefit, and complete removal of the kidney mitigates the risk of multifocal tumor recurrence in the native organs [12,13];
- Nephron-Sparing Surgery (NSS): for patients not yet on dialysis, NSS is the preferred option, particularly for small, localized, and exophytic tumors. This approach preserves native renal function, delays the onset of ESRD, and maintains eligibility for transplantation [12,13].

Histopathological examination of the resected specimen is critical. Confirmation of a low-grade, organ-confined tumor (pT1a) with negative surgical margins (R0 resection) provides the reassurance necessary for safe waitlisting.

Risk-stratified timing for transplantation

The traditional "one-size-fits-all" waiting period of 2-5 years has been superseded by a risk-adapted model [6,8]:

- Low-risk RCC (pT1a, ⩽ 3-4 cm, low grade): for tumors that meet these criteria, current guidelines from organizations like the European Renal Best Practice suggest that immediate waitlisting is acceptable [9,14]. The recurrence risk in this group is exceedingly low (< 2-3%), and the survival benefit of transplantation outweighs the negligible oncologic risk [5,10,15-18];
- Intermediate-risk RCC (pT1b-T2): a waiting period of approximately 2 years of disease-free observation is generally recommended to confirm oncologic stability;
- High-risk RCC (⩾ pT3, nodal involvement, high-grade features): a more cautious approach is warranted, typically requiring a minimum of 5 years of documented remission before considering transplantation. Metastatic disease remains an absolute contraindication [19,20].

This stratification is supported by multicenter studies, such as the analysis by Cognard et al., which identified clear cell histology, advanced stage, and high Fuhrman grade as key predictors of recurrence [10].

The dual role of immunosuppression

The choice of immunosuppressive regimen is a critical consideration:

- Calcineurin inhibitors (CNIs): CNIs like tacrolimus and cyclosporine have been implicated in pro-oncogenic pathways, potentially promoting angiogenesis and tumor progression through interactions with VEGF and TGF-β [21];
- mTOR inhibitors: sirolimus and everolimus provide effective immunosuppression while concurrently exerting antiproliferative and antiangiogenic effects by inhibiting the mTOR pathway. Meta-analyses and registry studies have associated mTOR inhibitor-based regimens with a significant reduction in the incidence of post-transplant malignancies, including RCC recurrence [22,23]. However, their use must be balanced against a higher incidence of adverse effects (e.g., dyslipidemia, proteinuria, impaired wound healing).

The importance of structured surveillance

These patients must be subjected to surveillance protocols that vary according to their risk profile:

- Low-risk patients: annual abdominal imaging (ultrasound, CT, or MRI) for the first 5 years, potentially transitioning to biennial imaging thereafter;
- High-risk patients: more intensive surveillance with cross-sectional imaging (CT or MRI) every 6 months for the first 2-3 years, followed by annual imaging.

Such dedicated protocols facilitate the early detection of recurrence at a manageable stage, improving survival outcomes [24-26]. The overall risk of recurrence in carefully selected patients remains low (< 5% at 5 years), and graft survival is comparable to that of transplant recipients without a cancer history [10].

CONCLUSIONS AND FUTURE DIRECTIONS

Kidney transplantation after curative treatment of RCC is a safe and effective strategy when guided by rigorous risk stratification and multidisciplinary management. For small, organ-confined tumors, mandatory waiting periods are obsolete and may unnecessarily compromise patient survival. The surgical approach must be individualized based on native renal function, and post-transplant care should incorporate tailored immunosuppression and lifelong surveillance. Future research should focus on prospective, multi-national registries to refine risk prediction. The integration of molecular biomarkers holds promise for distinguishing indolent from aggressive tumors. Furthermore, randomized trials are needed to definitively establish the optimal immunosuppressive strategy that balances graft function with oncologic safety. By embracing this evidence-based, personalized approach, we can ensure that a history of RCC does not unjustly deprive patients of the survival and quality-of-life benefits afforded by kidney transplantation.

Conflict of interest statement

The authors declare no conflict of interest.

Funding

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

Author contributions

All authors contributed equally to the conception, design, data collection, analysis, and writing of this manuscript. All authors read and approved the final version of the manuscript.

Ethical considerations

Not applicable.

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