MINI REVIEW

A descriptive overview of renal cell carcinoma and kidney transplantation

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ABSTRACT

Renal Cell Carcinoma (RCC) is more likely to develop in Kidney Transplant Recipients (KTRs) (RCC). The malignancy might appear at any point during the transplant process. RCC discovered during a transplant candidate's work-up requires therapy, and to reduce the chance of recurrence, a necessary monitoring period prior to transplantation is usually recommended. Candidates with small RCCs (less than 3 cm) who were discovered and removed by chance may skip the surveillance period. RCC in the donor organ, on the other hand, may not always limit use if the tumour is modest (between 2 cm and 4 cm) and resected with good margins prior to transplantation. 90% of RCCs are found in the native kidneys after transplantation, especially if acquired cystic kidney disease has occurred after continuous dialysis. After transplantation, no screening for RCC has been done discovered to be cost-effective RCC treatment in KTRs is difficult due to immunosuppression and oncologic medication modifications. Excision or nephrectomy is generally curative for confined RCC. Recent landmark trials in the non-transplanted population show that immunotherapy combinations improve survival in metastatic RCC patients. There are no dedicated trials in KTRs. A case series of immune checkpoint inhibitors in solid organ recipients with a variety of cancer types showed that one-third of the patients have a partial or complete tumour response, with rejection developing in 40% of the patients.

Key Words: *Kidney Transplant Recipients (KTRs); Renal Cell Carcinoma (RCC); Transplantation, Chronic Kidney Disease (CKD); Immunosuppression*

INTRODUCTION

Localized RCC is possibly curable with surgery alone, while recurrence occurs in 3%-30% of cases depending on stage [1] because of this tumour's natural resistance to standard chemotherapy and radiotherapy, the prognosis for metastasized or locally progressed disease has typically been low [2]. The previous few decades have brought new main therapy principles to the clinic, based on advancements in immuno-oncology and molecular tumour biology. First, immune system activity had been predicted for a long time. Since 1928, case reports have reported spontaneous remission of metastatic RCC after initial tumour nephrectomy [3]. However, early immunotherapy experiences, dating back to the mid-1980s, were unsuccessful. Until the mid-2000s, interleukin-2 or interferon alpha were employed to trigger anticancer immune responses, but modest response rates (7%-27%) and a high rate of toxicity dampened enthusiasm [4].

The second advancement in RCC treatment came from a better knowledge of the molecular processes that drive tumour growth. In a nutshell, both hereditary and sporadic clear-cell RCC has mutations that stimulate the VEGF receptor pathway [1]. Since FDA approval in 2005, Tyrosin-Kinase Inhibitors (TKI) and other VEGF receptor inhibitors, [5,6] as well as mechanistic (mammalian) target of rapamycin inhibitors, have influenced this system and increased progression-free and overall survival [7].

Finally, immunotherapy has become the first-line treatment since 2018. In comparison to the previous standard of care for metastatic RCC, a combination of two immune checkpoint inhibitors, such as nivolumab plus ipilimumab [8] or a combination of a checkpoint inhibitor and a TKI, such as pembrolizumab plus axitinib, was found to be superior as a first-line medical treatment in terms of progression-free survival, objective response rate, and overall survival. Both regimens are FDA-approved; albeit the former is intended for people who are at moderate or high risk [9]. There has been no head-to-head comparison of these combination regimens; however the European Association of Urology (EAU) recently updated guidelines suggest either as first-line therapy. There has been no systematic trial of immune checkpoint inhibitors in solid organ transplant recipients on immunosuppression.

DISCUSSION

Kidney transplantation is largely recognised as the best therapy option. Kidney transplantation is associated with increased survival [10] and quality of life and comes at a cheaper cost to society than being on the dialysis waiting list. Acute rejections have been decreased to less than 10%, and >90%-95% of grafts function beyond the first year because to modern medication [11]. In parallel, mortality has dropped to the point that 60%-80% of patients survive >10 years after receiving a first deceased or living donor kidney transplant [2]. Cardiovascular problems have typically dominated outcomes in these patients, but this has decreased to the point where malignancy and infectious disorders have become more common beyond the first year after transplantation [12]. According to a recent report from the European Renal Association-European Dialysis and Transplant Association, cancer mortality among elderly Kidney Transplant Recipients (KTRs) has increased alarmingly in recent decades [13] possibly due to the acceptance of more elderly and comorbid patients for kidney transplantation. This suggests that transplant doctors should place a greater emphasis on cancer early diagnosis and possible prevention.

In general, KTRs have a 2- to 4-fold higher risk of cancer than the general population, with the increased risk being most pronounced for cancers associated with UV radiation (i.e, skin cancer) and infection-related cancer but also extending to several cancer types unrelated to infection [14]. RCC is roughly 5-10 times more common in KTRs than in the general population with the majority of cases (90 percent) occurring in the native kidneys and only rarely in the kidney allograft [15]. The absolute risk of RCC in KTRs, on the other hand, is quite low. Kidney cancer is one of the most prevalent cancers in the general population, accounting for 5% of all cancers in men and 3% in women, with a peak incidence between 60-70 years of age [16]. Its prevalence increased in the last two to three decades before levelling off, which coincided with the development of radiological imaging and greater detection of lower-stage cancers. Older age, male gender, tobacco smoking, obesity, and ACKD are known risk factors for RCC, however evidence on diabetes, physical inactivity, nutritional variables, and occupational carcinogens is inconsistent. Smoking cessation and weight loss may be the most effective preventative strategies at a community level [17]. Although the majority of RCC cases are sporadic, 5%-8% of them are linked to genetic disorders, with ten germline syndromes now known. Patients with multiple or bilateral RCC, as well as those with concomitant disorders/phenotypes, should undergo genetic testing.

RCCs that develop in CKD are frequently multi-centric and bilateral; however

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they have a better prognosis than sporadic RCC. It's unclear if this is due to earlier detection or particular CKD-related issues. Although papillary RCC is more common than clear-cell RCC, the histologic appearance is similar to rare instances. Acquired cystic disease–associated RCC is a CKD-specific variation.

Successful kidney transplantation may reduce the size of cysts and the prevalence of ACKD, but whether it also reduces the long-term risk of RCC development in native kidneys is a matter of controversy. [18] Transplantation restores kidney function but increases the risk of cancer development due to immunosuppression. When compared to the general population, kidney cancer incidence was increased about 10-fold in patients on dialysis and after transplantation, whereas, reported an increased risk of kidney cancer (39%) early after transplant compared to patients on the waitlist. Cancer risks were compared between periods of dialysis and periods with a working graft in a recent research of almost 200 000 individuals from the Scientific Registry of Transplant Recipients. Because of the study's scale, it was possible to assess the risk of developing specific cancer types as well as the association between immunodeficiency and poor kidney function. During dialysis, the incidence of kidney cancer was obviously higher.

More than half of RCC cases are discovered early by radiologic imaging for other diseases or unspecific symptoms in the general population. [3] Due to the late onset of symptoms, approximately 25% of patients come with advanced disease after the tumour has migrated to surrounding structures. Paraneoplastic symptoms can be seen in about one-third of symptomatic patients, and are sometimes linked to the secretion of vasoactive peptides or hormones like parathyroid hormone–related protein, erythropoietin, gonadotropins, human chorionic somatosensory, adrenocorticotropic hormone–like substance, renin, glucagon, or insulin. Weight loss, night sweats, lethargy, oedema, liver failure, pain, cough, anaemia, erythrocytosis, hypercalcemia, and other metabolic abnormalities are all possible symptoms and findings. RCC was once known as the internist's tumour because of its various presentations; however, it has been renamed in the modern period.

CONCLUSION

There are no defined standards for assessing or treating cancers in renal allografts or RCC in KTRs. In practise, therapeutic procedures specified for the general population are employed with certain adjustments as long as they are appropriate. Localized RCC in defective native kidneys is frequently treated with nephrectomy; however numerous case reports show successful nephron sparing surgery or ablative therapy for localised RCC in allografts. RCC is more common in KTRs, especially in the native kidneys. Screening for RCC in all KTRs is not cost effective, however it may be useful in high-risk categories including those who have had a previous RCC or who have ACKD. Localized RCC is treated in the same way as non-transplanted RCC is. There is currently no trial evidence for the best immunosuppressive strategy or oncological treatment for advanced RCC. Randomized trials and prospectively gathered data are both urgently required.

REFERENCES

1. Cohen HT. McGovern fJ. Renal-cell carcinoma. N Engl J Med. 2005;353:2477-2490.
2. Griffith JJ, Amin KA, Waingankar N, et al. Solid renal masses in transplanted allograft kidneys: a closer look at the epidemiology and management. Am J Transplant. 2017;17:2775-2781.
3. Fernández-Pello S, Hora M, Kuusk T, et al. Management of sporadic renal angiomyolipomas: a systematic review of available evidence to guide recommendations from the European Association of Urology Renal Cell Carcinoma Guidelines Panel. Eur Urol Oncol. 2020;3:57-72.
4. Amato RJ. Chemotherapy for renal cell carcinoma**.** In Seminars oncol 2000;27:177-186.
5. Escudier B, Eisen T, Stadler WM, et al. Sorafenib in advanced clear-cell renal-cell carcinoma**.** Eng J Med. 2007;356:125-134.
6. Motzer RJ, Hutson TE, Tomczak P, et al. Sunitinib versus interferon alfa in metastatic renal-cell carcinoma**.** Eng J Med. 2007;356:115-124.
7. Hudes G, Carducci M, Tomczak P, et al. Temsirolimus, interferon alfa, or both for advanced renal-cell carcinoma**.** Eng J Med. 2007;356:2271-2281.
8. Motzer RJ, Tannir NM, McDermott DF, et al. Nivolumab plus ipilimumab versus sunitinib in advanced renal-cell carcinoma**.** Eng J Med. 2018.
9. Rini BI, Plimack ER, Stus V, et al. Pembrolizumab plus axitinib *versus* sunitinib for advanced renal-cell carcinoma. Eng J Med. 2019;380:1116-1127.
10. Wolfe RA, Ashby VB, Milford EL, et al. Comparison of mortality in all patients on dialysis, patients on dialysis awaiting transplantation, and recipients of a first cadaveric transplant. Eng J Med. 1999;341:1725-1730.
11. Saran R, Robinson B, Abbott KC, et al. United States renal data system. 2016 USRDS annual data report: Epidemiology of kidney disease in the United States**.** Natl Inst Diabetes Diges Kidney Dis. 2016.
12. Ying T, Shi B, Kelly PJ, et al. Death after kidney transplantation: An analysis by era and time post-transplant**.** J Am Soc Nephro. 2020;31:2887-2899.
13. Boenink R, Stel VS, Waldum-Grevbo BE, et al. Data from the ERA-EDTA Registry were examined for trends in excess mortality in European adults on kidney replacement therapy**.** Kidney Intern. 2020;98:999-1008.
14. Wong G, Hope RL, Howard K, et al. One-time fecal immunochemical screening for advanced colorectal neoplasia in patients with CKD. J Am Soc Nephro. 2019;30:1061-1072.
15. Leveridge M, Musquera M, Evans A, et al. Renal cell carcinoma in the native and allograft kidneys of renal transplant recipients**.** J Urol. 2011;186:219-223.
16. Tahbaz R, Schmid M, Merseburger AS. Prevention of kidney cancer incidence and recurrence: lifestyle, medication and nutrition. Current Opin Urol. 2018;28:62-79.
17. Dahle DO, Skauby M, Langberg CW, et al. Renal cell carcinoma and kidney transplantation: A narrative review. Transplant. 2022;106:52-63.
18. Yanik EL, Clarke CA, Snyder JJ, et al. Variation in cancer incidence among patients with ESRD during kidney function and nonfunction intervals. J Am Soc Nephrol. 2016;27:1495-1504.