Дослідницька стаття

Research Article

НИРКИ KIDNEYS

DOI: 10.65327/kidneys.v15i1.619

Vivekanandan J[1*], Dr Sarbjot Kaur,[2] Dr. Nimesh Kumar Tiwari[3], Dr. K. Parameswaran Namboothiri[4], Dr. Bhavya Khurana[5]

[1*]*Senior Resident, Department of Urology and Renal Transplantation, JSS Medical College, Mysore, Karnataka, India, Email ID: viveksurgeon@gmail.com Orcid ID: 0009-0007-4430-6924*

[2]*Assistant Professor- Radiation Oncology Guru Gobind Singh Medical College and Hospital, Faridkot Email ID - sarbjotsarb@gmail.com ORCID ID - 0009-0002-7605-3451*

[3]*Assistant Prof (Surgery) Command Hospital, Lucknow Email ID: nimeshtiwari26@gmail.com, ORCID ID: 0009-0009-0339-5830*

[4]*Professor & Head, Department of Panchakarma, Amrita School of Ayurveda, Amrita Vishwa Vidyapeetham, Amritapuri, Kerala, India, Email ID: nambu24@gmail.com ORCID ID 0000-0002-5348-6388*

[5]*Research Associate, Department of Translational Research, All India Institute of Ayurveda, bhavyakhurana1997bk@gmail.com ORCID ID - 0009-0004-6295-6144*

Diagnostic and Therapeutic Innovations in Renal Cell Carcinoma: A Urologic Oncology Review

For citation: Kidneys. 2026;15(1):265-274. Acceptance- 27/01/2026

Received- 03/01/2026 Doi: 10.65327/kidneys.v15i1.619

Abstract

Renal cell carcinoma (RCC) is a biologically heterogeneous disease. In the recent past, the clinical management of RCC has been redefined by the new development of diagnostic imaging, molecular and genetic profiling. The following review attempts to provide the current events in diagnosing, risk stratification, and management of RCC through the lens of nephrology. A literature review was performed thoroughly with the emphasis on the developments in imaging modalities, molecular and genetic diagnostics, prognostic models, and novel therapeutic methods. Literary evidence of clinical trials, systematic reviews, and international guidelines was analyzed. The result showed that imaging and radiomics advances have enhanced the characterization of tumors and the assessment of risks associated with RCC, whereas molecular and genetic diagnostics have allowed a fine classification of the disease. The Therapeutic interventions, such as setting up targeted therapy, immunotherapy and minimally invasive surgery procedures, have taken a huge step forward in oncologic outcomes. The changes in the management of RCC over the years, the concept of advanced diagnostics, along with the modern modalities, have revolutionized the management process of this cancer. Oncologic efficacy should be offset with renal preservation by using multidisciplinary nephrology-centered approaches. Additional studies and fair practice of precision medicine is also essential to ensure better outcomes and life of patients with RCC.

Keywords: Renal cell carcinoma, Precision medicine, Molecular diagnostics, Risk stratification, Nephron-sparing therapy

Introduction

Kidney cancers have diagnostic and therapeutic problems which are unique due to their biological heterogeneity and their proximity to renal functions. Early disease infestation is usually asymptomatic and allows for less time to diagnose and intervene with a curative measure. Conventional diagnostic procedures and treatment plans are often inadequate to describe the heterogeneity of tumors, or they no longer contribute to targeted therapy. Simultaneously the important physiologic role of the kidney should be taken into consideration when choosing surgical or systemic therapy because disease and treatment can deteriorate the renal functions. These shortcomings underscore the increasing demand of new diagnostic instruments that can be used to enhance tumor detection, characterization and risk stratification. Equally, there is need to develop therapeutic modalities that can increase treatment efficacy but at the same time the kidney functions and toxicity should be reduced. All these problems make it necessary to proceed with innovative work in the diagnosis and treatment of kidney malignancies.

Renal cell carcinoma (RCC) is the primary product of malignancy of the kidney and it represents about 85-90 percent of all cases of renal cancer in the world. In particular, combination regimens based on immunology have completely transformed the treatment environment of advanced renal cell carcinoma [1,2]. Major randomized clinical trials prove better survival rates with immune checkpoint-inhibitor-based therapy compared to those with conventional monotherapy with

For correspondence: Vivekanandan J, Senior Resident, Department of Urology and Renal Transplantation, JSS Medical College, Mysore, Karnataka, India JSS University, Mysore, Karnataka, India Email ID: viveksurgeon@gmail.com Orcid ID(if you have) : 0009-0007-4430-6924

Full list of authors information is available at the end of the article.

tyrosine kinase inhibitors [3,4]. Renal cell carcinoma affects directly renal anatomy and renal functioning and sometimes surgical intervention, systemic therapy, or both may be required. Combination regimens are complemented with the addition of the targeted therapy and immunotherapy to improve progression-free and overall survival in a myriad of disease settings [5,6]. Additionally, post-nephrectomy adjuvant immunotherapy has emerged as an effective strategy for reducing the risk of recurrence in patients with high-risk localized disease [7]. Therapeutic progress, proper diagnosis, risk stratification, and individualization of treatment are not easy despite the therapeutic advancements. The new technologies in diagnostics, such as molecular imaging and liquid biopsy methods are opening up scope for early detection and better characterization of the disease [8,9]. Thus, it is important to evaluate the latest diagnostic and treatment advances in renal cell carcinoma to support clinical judgment and interdisciplinary care. Recent clinical recommendations focus on risk-specific management approaches and heterogeneity of the disease restricts the quality of prognostic models and treatment choices [10]. The current liquid biopsy method and especially circulating tumor DNA (ctDNA) is shown to have potential in prognostication and disease monitoring in renal cell carcinoma, but the sensitivity depends on the disease stage [11]. Advances in metastasis-directed radiotherapy for oligometastatic clear-cell renal cell carcinoma introduce new treatment paradigms but require further validation before widespread clinical adoption [12]. Prognostic associations between circulating tumor DNA levels and clinical outcomes further support the potential role of liquid biopsy in surgically resected renal cell carcinoma [13]. Radiomics-based analysis of computed tomography and magnetic resonance imaging improves non-invasive tumor characterization and prognostic assessment in renal cell carcinoma [14,15]. Narrative and systematic reviews further support the growing role of radiomics and artificial intelligence-based imaging in predicting treatment response and oncological outcomes [16,17]. Emerging biomarker strategies, including circulating tumor cells (CTCs), enhance understanding of tumor biology and provide complementary value to circulating tumor DNA-based approaches [18]. Machine learning enhanced radiomic models add incremental prognostic value beyond existing clinical risk models [19]. Recent meta-analyses also demonstrate the feasibility of non-invasive prediction of nuclear grade in renal cell carcinoma using computed tomography-based radiomics [20].

Although these technological advances are present, there are a number of significant issues that still restrict their extensive usage in the clinical context. Lots of radiomic and machine learning models are still limited to research only because they are not standardized, imaging protocols vary, and they are not validated in large different populations of patients. Variations in scanner, image acquisition, and segmentation techniques decrease the reproducibility and comparison between studies. Moreover, the incorporation of advanced imaging biomarkers into standard clinical activities is still complicated and it takes special skills and computer resources, which are not always accessible. Clinicians are unsure of the way radiomic outputs should be interpreted and utilized with established clinical and pathological risk factors in the best way possible. These shortcomings have provided a case to harmonise the methodologies, prospective validation and models that are clinically interpretable to ensure that diagnostic innovations add substantial value to patient care and therapeutic decision-making in renal cell carcinoma.

Objectives of the Study:

1. To review recent advances in the diagnosis, risk stratification, and management of renal cell carcinoma
2. To evaluate the role of molecular, imaging, and prognostic tools in personalized RCC care
3. To highlight nephrology-focused strategies aimed at preserving renal function while optimizing oncologic outcomes

Methods

Literature Search Strategy

A comprehensive literature search was conducted to identify studies reporting diagnostic and therapeutic innovations in renal cell carcinoma. Electronic databases such as PubMed/MEDLINE, Scopus, and Web of Science were used. The search was limited to the past seven years 2018 to 2025 to guarantee the availability of current and clinically relevant studies. Search terms were joined by using Boolean operators and comprised of keywords such as renal cell carcinoma, kidney cancer, diagnostic innovations, advanced imaging, molecular biomarkers, targeted therapy, immunotherapy, nephron-sparing surgery, and renal toxicity. Manual screening of the reference lists of the selected articles was done to find relevant publications, clinical, translational and experimental research related to nephrology and urology were also included**.**

Study Selection Criteria

The studies were included based on predetermined inclusion and exclusion criteria. Articles that could be included in the study were the original research articles, randomized and non-randomized clinical trials, observational studies, systematic reviews, meta-analyses, international clinical guidelines on renal cell carcinoma diagnostics and treatment methods. Articles which showed applicability to kidney disease, renal functioning maintenance or urologic oncology were included. The exclusion criteria included conference abstracts that were not full papers, editorials without substantial data, non-peer-reviewed articles, case reports, and studies that were older than seven years.

Data Mining and Generalization

The included studies provided relevant information, which was extracted in terms of diagnostic methods, treatment approaches, clinical outcomes, and renal functioning implications. The information that was extracted covered the study design, patient population, diagnostic modality, therapeutic intervention and the

main findings. Due to the diversity of the study designs and the results that were reported, a narrative synthesis method was used. The data were categorized in themes of diagnostic innovations, therapeutic developments and considerations of nephrology. A comparative analysis was conducted in order to reveal the tendencies, strong points, weaknesses, and gaps in the literature. This methodology allowed synthesizing existing evidence in an integrated and clinically meaningful way that was applicable to nephrologists, urologists, and researchers in the renal field.

Scope and Conceptual Framework of the Review

The review was constructed as a narrative synthesis of emerging data in a manner that reflected a synthesis of the current evidence to bring the emerging diagnostic modalities, changing treatment modalities, and considerations that nephrology has with the management of renal cell carcinoma. The focus was put on clinically meaningful innovations, such as innovations in imaging, molecular profiling, target and immune-based therapies, and modalities intended to maintain renal functionality. In this way, the analysis of the current trends, unmet needs and potential future directions in the field of renal cell carcinoma care was achieved both under urologic and nephrologic perspective.

Overview of Renal Cell Carcinoma

Renal cell carcinoma (RCC) comprises a heterogeneous group of malignancies arising from the renal tubular epithelium and exhibits substantial variation in histological and biological behavior. At the pathophysiological stage, RCC has a natural abnormality in angiogenesis, immune modulation, and cellular metabolic changes. Uncommon clinical findings have been made of spontaneous or dramatic regression of tumors with systemic inflammatory responses following targeted therapy, which can be explained by the complicated nature of the interplay between the biology of the tumors and the host immune response [21]. Nevertheless, the activation of the immune can also have a negative influence on the renal tissue. Case-studies show that the use of immune checkpoint inhibitor therapy can trigger acute tubulointerstitial nephritis by the immune cells infiltrating the renal parenchyma [22]. The increased number of multicenter studies also proves that immune checkpoint inhibitor-related acute kidney injury is a clinically significant complication and should be monitored and managed with special care [23]. Novel treatment modalities look into combination therapy to enhance the efficacy of treatment. There is case-based evidence that proposes the potential advantages of immunotherapy and chemotherapy combination in specific locally advanced renal and urothelial malignancies [24]. The current trend in systemic therapy for RCC increasingly emphasizes targeted therapies and immunotherapy, with a focus on balancing oncologic efficacy with renal safety and long-term preservation of kidney function [25].

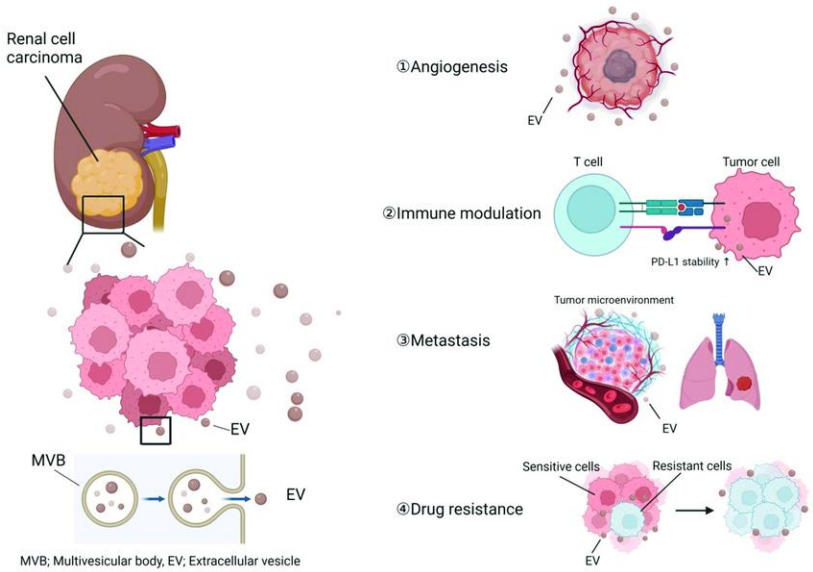

Figure 1: Extracellular Vesicles in the Pathophysiology and Progression of Renal Cell Carcinoma
Source: Takeda M et al., Nanomaterials, 2023;13:1611. DOI: 10.3390/nano13101611 [26]

Figure 1 indicates the key functions of extracellular vesicles that cancerous renal cells secrete during cancer progression. Extracellular vesicles facilitate dysfunctional angiogenesis, immune regulation in the tumor bed, metastatic spread, and drug resistant formation.

Diagnostic Innovations in Renal Cell Carcinoma

Recent New developments in diagnostic approaches have led to substantial diagnosing, characterizing, and treatment of renal cell carcinoma (RCC). Conventional diagnostic methods were based on the traditional imaging and histopathological analysis nevertheless, these techniques are often insufficient to obtain the heterogeneity and molecular complexity of the tumor. Simultaneously, united imaging standards like the Bosniak classification (version 2019) have enhanced the

diagnosing and treating cystic renal masses by enhancing reporting and risk grouping [27]. Moreover, better awareness of renal imaging mimic and there has been growing relevance to minimize misclassification and inappropriate treatment [28]. Together, these advancements have precursors to early detection, enhanced characterization, and less risky longitudinal observation, especially in the nephrology environment where renal functional preservation is one of the priorities.

Imaging Advances

Imaging continues to play a crucial role in the process of RCC diagnosis and staging, additionally, the latest innovations continue to mainstream its use in the clinical context. Diffusion-weighted imaging and perfusion techniques are considered functional imaging, which offers data about the cellularity and and the base of high-level quantitative analysis. Radiomics makes it possible to extract imaging features that cannot be observed visually and assists in the prediction of tumor grade, treatment response, and prognosis [29]. Artificial intelligence, which supports imaging, has more recently increased the number of applications in urinary tumors, including automated lesion classification, decision-making, and tailored treatment strategies [30]. These non-invasive techniques can be used jointly to decrease the need to perform repeated biopsies and enhance longitudinal surveillance, especially in cases where the patient uses a nephron-sparing approach or in patients with impaired renal functioning.

Molecular and Genetic Diagnostics

The use of molecular and genetic diagnostics has changed the way renal cell carcinoma is perceived and allowed for a more precise diagnosis of this disease. Genomic profiling detects important molecular changes that are entailed in tumor growth, angiogenesis, and immune evasion in favor of targeted therapy. Such approaches as circulating tumor cells and circulating tumor DNA are liquid biopsy techniques that provide the minimally invasive disease monitoring and prognostic models. Such methods enable the evaluation of the tumor dynamics in real time and could reveal a possibility of changes in molecular features linked with treatment resistance. Combined with the imaging results, molecular and genetic diagnostics allow completing the evaluation of RCC and make it individualized, which is in line with the premises of the practice of precision medicine [31].

Risk Stratification and Early Detection

Correct stratification of risk is very critical in order to maximize the management strategies in renal cell carcinoma. The predictive models based on a combination of clinical variables, imaging characteristics, and molecular data can assist in determining much higher-risk patients of the disease progression or reoccurrence. Specifically, radiomics in MRI has been observed to have an important role in preoperative staging, size, grade and necrosis prediction, and has become more valuable to assess non-invasive risks more precisely [32]. Prognostic markers allow distinguishing between indolent and aggressive tumors, which allows monitoring the intensity of surveillance and treatment intervention. The advantage of early detection strategies is that, using a combination of advanced imaging with biomarker-based assessment, there is enhancement, which identifies the clinically significant disease at an earlier stage. These methods contribute to interventional interruptions in good time and reduce overtreatment. Refined risk stratification has been shown to play a particularly beneficial role in nephrology-focused care, by expensive treatment escalation, and appropriate choice of the nephron-conservative treatment. Table 1 provides the brief overview of the main diagnostic advances in renal cell carcinoma, combining the development of imaging, molecular diagnostics, and risk estimates. It emphasizes the benefits of the standard and modern imaging modes, such as radiomics and artificial intelligence, in characterizing tumors and prognostic evaluation.

Table 1: Diagnostic Innovations in Renal Cell Carcinoma

Diagnostic Domain	Technique / Tool	Key Information Provided	Clinical Utility	Nephrology-Relevant Benefit
Conventional Imaging	CT / MRI	Tumor size, location, vascularity	Diagnosis and staging	Baseline assessment with non-invasive evaluation
Standardized Imaging Frameworks	Bosniak Classification (v2019)	Cystic lesion risk stratification	Management guidance	Avoids unnecessary surgery
Functional Imaging	DWI, Perfusion MRI	Tumor cellularity, angiogenesis	Tumor characterization	Reduces need for biopsy
Radiomics	Quantitative feature extraction	Tumor grade, prognosis prediction	Risk stratification	Supports nephron-sparing decisions
AI-Assisted Imaging	Machine learning models	Automated lesion classification	Decision support	Enables longitudinal monitoring
Genomic Profiling	Tumor DNA sequencing	Molecular alterations, pathways	Targeted therapy selection	Personalized treatment planning
Liquid Biopsy	ctDNA, CTCs	Tumor dynamics, resistance markers	Disease monitoring	Minimally invasive surveillance
Biomarkers	Blood/urine/tissue markers	Prognostic and predictive signals	Early detection	Renal-safe risk assessment

Integrated Risk Models	Clinical + imaging + molecular data	Progression and recurrence risk	Surveillance tailoring	Preserves renal function

Source: *Compiled from peer-reviewed studies on imaging advances, radiomics, artificial intelligence, and molecular diagnostics in renal cell carcinoma*

Therapeutic Innovations

The management of renal cell carcinoma has evolved at high rates in the past few years with some of the latest drugs, immunotherapies and methods of surgeries. Through these inventions, there has been a better chance of survival and wider range of treatment choices of a disease at any level. The development of contemporary therapeutic approaches and practices puts increased focus on individualized selection of treatment choices, which varies and depends on tumor biology, patient features, and credits state of renal functioning in accordance with recognized prognostic factors and risk models in renal cell carcinoma [33]. Combination of the systemic therapies with the surgical methods and minimally invasive methods allow more thorough management of the disease. Nonetheless, despite ongoing advances, concerns regarding toxicity and long-term kidney health persist, underscoring the need for a multidisciplinary approach.

Targeted Therapies

Treatment with specific therapy is one of the pillars of renal cell carcinoma. Tumor angiogenesis can effectively be blocked using agents that inhibit vascular endothelial growth factor pathways and tyrosine kinase signaling. There are other mechanisms of suppressing tumor growth and metabolism by mammalian target of rapamycin inhibitors. These therapies have shown great clinical utility especially in metastatic disease and advanced disease. Dosage schedules and patient identification will always be crucial to achieve the highest benefit of the therapy without interference with the renal performance, especially combined with nephron-sparing and minimally invasive surgery [34].

Immunotherapy

Immunotherapy treatment has brought change to the treatment of renal cell carcinoma because it uses the host immune system to regulate growth of the tumor. Diegetic immunochemotherapy has been shown to enhance survival and suppress cancer tumor invasion by using the immune checkpoint blocking programmed cell death pathways. Combination regimens that include immunotherapy using targeted agents can promote further efficacy but could potentially be more toxic and this is especially important in cases featuring perioperative and high-risk disease (or both) [35]. Renal complications are one of the adverse events associated with immunity that should be taken into account within the clinical practice. Proper patient selection, early toxicity detection, coordinated efforts of nephrologists and oncologists are essential in safe and effective administration of immunotherapies.

Surgical and Minimally Invasive Approaches

One of the most important interventions in the management of renal cell carcinoma is surgery, especially in the localized disease. Nephron-sparing operation is expected to attain oncologic renal cortex which maintains renal functioning and lessens chances of chronic kidney illness. The development of robotic-assisted and minimally invasive surgeries has enhanced surgical accuracy, decreased the morbidity of the perioperative period, and decreased the time of recovery due to greater knowledge in tumor biology and molecular heterogeneity [36]. Ablative methods provide alternative solutions to selected patients who cannot be well-operated upon with results progressively based on sophisticated pathology staging systems [37]. These are strategies that are consistent with the nephrology-focused care that emphasizes long-term preservation of the kidneys along with effective management of tumor. Table 2 gives an organized view of the key therapeutic developments in renal cell carcinoma which are inclusive of targeted treatments, immunotherapy, surgical and minimally invasive treatments. It emphasizes action mechanisms, clinical manifestations and settings of therapy in various stages of the disease. Specific attention is paid to addressing the renal and nephrology-related issues, such as the risk of nephrotoxicity, the maintenance of renal functions, and patient selection. The table allows comparison of both systemic and local remedies in the context of a multidisciplinary care approach.

Table 2: Therapeutic Innovations in Renal Cell Carcinoma

Therapeutic Modality	**Examples / Techniques**	**Mechanism of Action**	**Clinical Indications**	**Renal & Nephrology Considerations**
Targeted Therapies	VEGF inhibitors, TKIs, mTOR inhibitors	Inhibition of angiogenesis and tumor growth pathways	Advanced and metastatic RCC	Risk of nephrotoxicity; requires dose adjustment and monitoring
Immunotherapy	PD-1 / PD-L1 inhibitors, combination regimens	Restoration of antitumor immune response	Advanced and high-risk RCC	Immune-related renal adverse events; multidisciplinary oversight needed
Combination Therapy	Immunotherapy + targeted agents	Synergistic tumor control	High-risk and metastatic disease	Increased toxicity; careful patient selection
Nephron-Sparing Surgery	Partial nephrectomy	Local tumor excision with renal preservation	Localized RCC	Reduces risk of chronic kidney disease

Robotic & Minimally Invasive Surgery	Robotic-assisted partial nephrectomy	Precision surgery with reduced morbidity	Complex localized tumors	Faster recovery, renal preservation
Ablative Techniques	Cryoablation, radiofrequency ablation	Local tumor destruction	Poor surgical candidates	Minimally invasive, renal-safe alternatives

Source: Compiled from peer-reviewed studies and reviews on therapeutic strategies and surgical management of renal cell carcinoma

Nephrology-Focused Considerations

One of the core concerns in the treatment of renal cell carcinoma (RCC) involves preserving renal functionality since the disease and the agents used to treat it may have a significant impact on the well-being of the kidneys. A considerable number of RCC patients go to the hospital with renal impairment. They are at a greater risk of developing chronic kidney disease after intervention. Such therapies as immunotherapy and targeted therapy can cause nephrotoxicity due to hemodynamic adjustments, immune-driven damage, or accumulation of stress in the kidneys and require close monitoring and prompt treatment. In metastatic RCC, prognostic factors are more firmly laid down, and risk-adapted treatment options are offered to enable clinicians to adjust the intensity of the treatment, taking into consideration the renal vulnerability [38]. Although surgical treatments are potentially curative in focal disease, further depletion of renal reserve can occur, especially with the need to do radical renal surgery. Therefore, the nephron-sparing treatment and the conservative management methods are given the first priority whenever it can be done oncologically. Renal injury caused by treatment can worsen the chronic renal disease progression, which will impact on the quality of life and survival in the long run. Dose adjustment, ethics of hydration, preventive use of nephrotoxic substances and close biochemical monitoring all should be implemented as nephroprotective measures to prevent these risks. The interdisciplinary partnership of the oncologists, nephrologists and urologists is of crucial importance in terms of detection and treatment of the renal complications. This coordinated care especially applies to patients who are undergoing active surveillance or conservative management of small renal masses, whereby the maintenance of renal functioning is one of the main therapeutic objectives of the treatment [39].

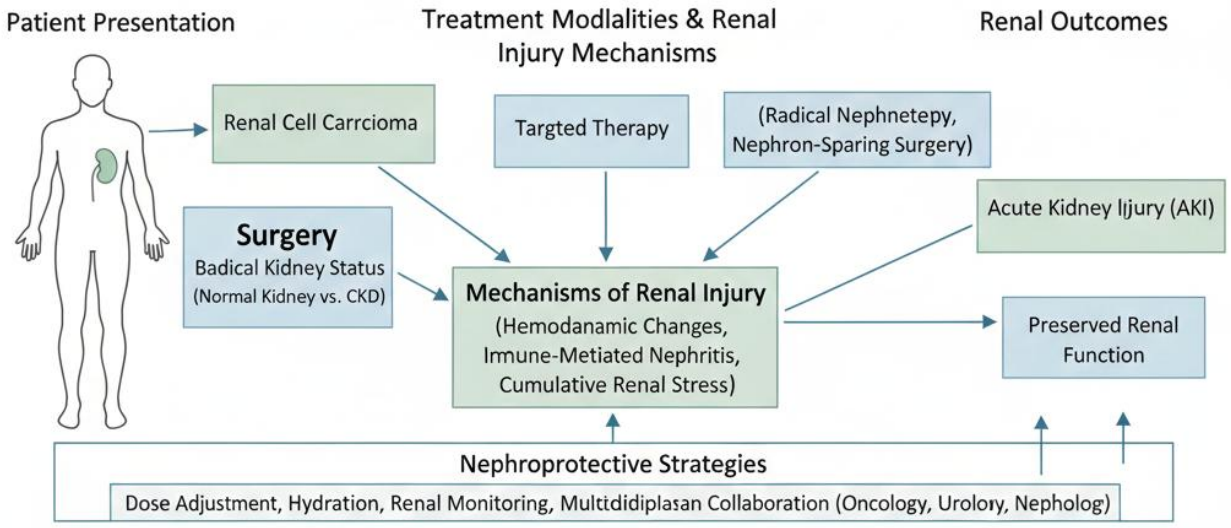

Figure 2: Nephrology-Focused Management Framework in Renal Cell Carcinoma: Treatment-Related Renal Injury Mechanisms and Outcomes

Source: Created by the authors based on a synthesis of published literature and clinical practice guidelines in nephrology and oncology.

Figure 2 presents a nephrology-based model on the management of renal cell carcinoma. It provides an outline of the role of patient baseline renal status and treatment modalities such as surgery and targeted therapy in renal injury mechanisms. The mechanisms include hemodynamic changes, immune-mediated nephritis and accumulative renal stress. The figure shows the possible outcomes of renal failure including acute kidney injury or preservation of renal function. Nephroprotective strategies are stressed as a focal point

of renal damage reduction and enhancing patient outcomes.

Nephrotoxicity Monitoring and Biomarker-Guided Renal Assessment

The development of renal biomarkers is an encouraging breakthrough in the identification of nephrotoxicity and risk classification. Neutrophil gelatinase-associated lipocalin (NGAL), kidney injury molecule-1 (KIM-1) and cystatin C are some examples of biomarkers that have demonstrated early detection of acute kidney injury and immune-mediated nephritis compared to conventional outcomes. Such indicators will become particularly useful in patients undergoing immune checkpoint inhibitors treatment, where the toxicity of the renal system can manifest within a short time. Such a combination of clinical parameters, laboratory biomarkers, and radiography findings allow a more effective assessment of kidney susceptibility to help with precision oncology and risk-based decision-making on therapeutic choices, and maintain long-term renal functionality. Table 3 provides a summary of the important parameters of renal monitoring that are employed to monitor nephrotoxicity in patients with renal cell carcinoma. It illuminates the traditional renal-based test results and the developing biomarkers, which aid in the early identification of kidney injury.

Table 3. Renal Monitoring Parameters and Biomarkers for Nephrotoxicity Assessment in Renal Cell Carcinoma

Assessment Category	Parameter / Biomarker	Clinical Relevance	Utility in RCC Management
Conventional Renal Function Markers	Serum creatinine	Indicator of overall renal filtration	Baseline renal assessment and longitudinal monitoring
	Estimated glomerular filtration rate (eGFR)	Reflects kidney function reserve	Guides treatment selection and dose adjustment
Urinary Markers	Proteinuria	Marker of glomerular injury	Particularly relevant for VEGF-targeted therapies
	Urinalysis (sediment)	Detects tubular or inflammatory injury	Early identification of renal toxicity
Emerging Renal Biomarkers	NGAL (Neutrophil gelatinase-associated lipocalin)	Early marker of acute kidney injury	Detects subclinical nephrotoxicity
	KIM-1 (Kidney injury molecule-1)	Marker of tubular damage	Useful in therapy-related renal injury
	Cystatin C	Sensitive indicator of GFR changes	Less influenced by muscle mass than creatinine
Immunotherapy-Related Markers	Inflammatory markers (e.g., eosinophilia)	Suggest immune-mediated nephritis	Supports early detection of immune-related adverse events
Imaging-Based Assessment	Renal ultrasound / CT	Structural evaluation of renal parenchyma	Identifies obstruction, scarring, or volume loss
Integrated Monitoring Approach	Combined clinical, laboratory, and imaging data	Comprehensive renal risk evaluation	Supports personalized and risk-adapted RCC management

Source: Created by the authors based on a synthesis of published literature and current clinical practice guidelines in nephrology and urologic oncology.

Management Challenges

Management of renal cell carcinoma faces still faces existing challenges. The issue of therapeutic resistance has been a significant challenge, and is in large part due to tumor heterogeneity and the dynamic nature of tumor-cell evolution in response to treatment effects, which allow cancer cells to circumvent treatment effects [40]. This resistance usually minimizes the persistence of clinical responses and makes them regularly change therapy. Toxicity due to the treatment is also another issue, where the side effects may interfere with patient compliance, as well as negatively affecting renal function, especially in individuals with underlying kidney disease. In addition, renal cancer cells reprogram metabolism, which leads to the pathogenesis and difficulties with the effectiveness of continuous treatment [41]. There is still a considerable gap in knowledge concerning the ideal sequencing and combination of the available therapies, their long-term renal outcome and overall survival. Economic determinants can significantly be seen as obstacles as well, and their availability is limited to a great number of healthcare facilities due to the high cost of treatment and a lack of access to advanced diagnostics and innovative treatments. Nanotechnological research, optimisation of clinical guidelines and incorporation of fair and patient-focused healthcare interventions will be needed to overcome these issues.

Future Directions

It is assumed that future developments in the treatment of renal cell carcinoma (RCC) will focus more and more on the development of risk-adaptive and more individualized treatment regimes that will optimize both the oncologic outcomes and ensure renal survival over the long term. Better characterization of small foci of renal disease by fine-tuning clinical evaluation, developments in imaging, and focused treatment will

enable tailored treatment and prevent excessive treatment to the indolent disease [42]. Advances in the prognostic model will continue to be a major research area especially among patients who have high-risk localised and locally advanced RCC. Strong predictive models that incorporate clinical, pathological, and molecular factors could be used to improve the detection of patients at higher risk of relapse or early disease recurrence to inform decisions related to surveillance and adjuvant treatment after the surgical resection [43]. Active surveillance is also anticipated to widen its role and this is with patients who are carefully chosen with localized small renal masses. The evidence supporting surveillance-based strategies indicates that intervention may be delayed or avoided without compromising oncologic outcomes, while preserving renal function and quality of life [44]. Simultaneously, the ongoing development of guideline-based imaging plans will enhance the level of accuracy of the diagnosis process, risk classification, and follow-up of the presence of renal masses. onsistency in decision-making and multidisciplinary care will be enhanced through the use of standardized imaging procedures aligned with clinical guidelines [45]. All these future prospects highlight the significance of incorporating the risk stratification, surveillance, and nephroprotective approaches to propel precision medicine in RCC.

Conclusion

Renal cell carcinoma is a complex and heterogeneous malignancy that requires a multidisciplinary approach for optimal management. The innovations in diagnostic imaging, molecular and genetic profiling, and risk stratification have significantly enhanced the characterization of tumors, which has led to earlier identification of the disease and more accurate evaluation of the disease behavior. This progression informs personalized clinical decision-making, enabling distinction between indolent and aggressive tumors, thereby minimizing unnecessary interventions while ensuring timely treatment for high-risk patients. RCC therapy has changed the contemporary world of treatment, with specific therapy, immunotherapy, and minimal invasive surgery techniques that have advanced the survival rates in patients at different stages of the disease in a great way. The growing focus on the nephron-sparing strategies indicates the recognition of the significance of maintaining renal functioning and has not sacrificed the control of oncologic achievements. Meanwhile, the trends of increased usage of systemic therapy and combination dosages emphasize the importance of careful patient monitoring of treatment associated with toxicity especially renal. Considerations of nephrology are at the center of the current RCC management because several patients are initially diagnosed with kidney disease or renal failure after the treatment. There should be shared management between the oncologist, the urologist, the radiologist, and the nephrologist to moderate between the therapeutic effectiveness and the kidney health.

References

[1] Motzer RJ, Tannir NM, McDermott DF, Arén Frontera O, Melichar B, Choueiri TK, Plimack ER, Barthélémy P, Porta C, George S, Powles T. Nivolumab plus ipilimumab versus sunitinib in advanced renal-cell carcinoma. New England Journal of Medicine. 2018 Apr 5;378(14):1277-90. DOI: 10.1056/NEJMoa1712126

[2] Rini BI, Plimack ER, Stus V, Gafanov R, Hawkins R, Nosov D, Pouliot F, Alekseev B, Soulières D, Melichar B, Vynnychenko I. Pembrolizumab plus axitinib versus sunitinib for advanced renal-cell carcinoma. New England Journal of Medicine. 2019 Mar 21;380(12):1116-27. DOI: 10.1056/NEJMoa1816714

[3] Motzer RJ, Penkov K, Haanen J, Rini B, Albiges L, Campbell MT, Venugopal B, Kollmannsberger C, Negrier S, Uemura M, Lee JL. Avelumab plus axitinib versus sunitinib for advanced renal-cell carcinoma. New England Journal of Medicine. 2019 Mar 21;380(12):1103-15. DOI: 10.1056/NEJMoa1816047

[4] Powles T, Plimack ER, Soulières D, Waddell T, Stus V, Gafanov R, Nosov D, Pouliot F, Melichar B, Vynnychenko I, Azevedo SJ. Pembrolizumab plus axitinib versus sunitinib monotherapy as first-line treatment of advanced renal cell carcinoma (KEYNOTE-426): extended follow-up from a randomised, open-label, phase 3 trial. The Lancet Oncology. 2020 Dec 1;21(12):1563-73. 10. DOI 1016/S1470-2045(20)30436-8

[5] Motzer R, Alekseev B, Rha SY, Porta C, Eto M, Powles T, Grünwald V, Hutson TE, Kopyltsov E, Méndez-Vidal MJ, Kozlov V. Lenvatinib plus pembrolizumab or everolimus for advanced renal cell carcinoma. New England Journal of Medicine. 2021 Apr 8;384(14):1289-300. DOI: 10.1056/NEJMoa203571

[6] Choueiri TK, Powles T, Burotto M, Escudier B, Bourlon MT, Zurawski B, Oyervides Juárez VM, Hsieh JJ, Basso U, Shah AY, Suárez C. Nivolumab plus cabozantinib versus sunitinib for advanced renal-cell carcinoma. New England journal of medicine. 2021 Mar 4;384(9):829-41. DOI: 10.1056/NEJMoa2026982

[7] Choueiri TK, Tomczak P, Park SH, Venugopal B, Ferguson T, Chang YH, Hajek J, Symeonides SN, Lee JL, Sarwar N, Thiery-Vuillemin A. Adjuvant pembrolizumab after nephrectomy in renal-cell carcinoma. New England Journal of Medicine. 2021 Aug 19;385(8):683-94. DOI: 10.1056/NEJMoa210639

[8] Shuch B, Pantuck AJ, Bernhard JC, Morris MA, Master V, Scott AM, Van Praet C, Bailly C, Önal B, Aksoy T, Merkx R. [89Zr] Zr-girentuximab for PET–CT imaging of clear-cell renal cell carcinoma: a prospective, open-label, multicentre, phase 3 trial. The Lancet Oncology. 2024 Oct 1;25(10):1277-87. DOI: 10.1016/S1470-2045(24)00402-9

[9] Powles T, Choueiri TK, Albiges L, Peltola K, de Velasco G, Burotto M, Suarez C, Ghatalia P, Iacovelli R, Lam ET, Verzoni E. Health-related

quality of life with belzutifan versus everolimus for advanced renal cell carcinoma (LITESPARK-005): patient-reported outcomes from a randomised, open-label, phase 3 trial. The Lancet Oncology. 2025 Apr 1;26(4):491-502. DOI: 10.1016/S1470-2045(25)00032-4

[10] Motzer RJ, Jonasch E, Agarwal N, Alva A, Bagshaw H, Baine M, Beckermann K, Carlo MI, Choueiri TK, Costello BA, Derweesh IH. NCCN Guidelines® insights: kidney cancer, version 2.2024: featured updates to the NCCN Guidelines. Journal of the National Comprehensive Cancer Network. 2024 Feb 1;22(1):4-16. DOI: 10.6004/jnccn.2024.0008.

[11] Geertsen L, Koldby KM, Thomassen M, Kruse T, Lund L. Circulating tumor DNA in patients with renal cell carcinoma. A systematic review of the literature. European Urology Open Science. 2022 Mar 1;37:27-35. https://doi.org/10.1016/j.euros.2021.12.006

[12] Tang C, Sherry AD, Seo A, Hara K, Choi H, Liu S, Sun X, Montoya A, Ludmir EB, Shah AY, Jonasch E. Metastasis-directed radiotherapy without systemic therapy for oligometastatic clear-cell renal-cell carcinoma: primary efficacy analysis of a single-arm, single-centre, phase 2 trial. The Lancet Oncology. 2025 Oct 1;26(10):1289-99. DOI : 10.1016/S1470-2045(25)00380-8

[13] Correa AF, Kalashnikova E, Wu HT, Winters RM, Balcioglu M, Sudhaman S, Connolly DC, Gong Y, Uzzo RG, Sethi H, ElNaggar AC. Association of circulating tumor DNA with patient prognosis in surgically resected renal cell carcinoma. The Oncologist. 2024 Oct;29(10):887-93. https://doi.org/10.1093/oncolo/oyae180

[14] Ursprung S, Beer L, Bruining A, Woitek R, Stewart GD, Gallagher FA, Sala E. Radiomics of computed tomography and magnetic resonance imaging in renal cell carcinoma a systematic review and meta-analysis. European radiology. 2020 Jun;30(6):3558-66. DOI https://doi.org/10.1007/s00330-020-06666-3

[15] Mühlbauer J, Egen L, Kowalewski KF, Grilli M, Walach MT, Westhoff N, Nuhn P, Laqua FC, Baessler B, Kriegmair MC. Radiomics in renal cell carcinoma a systematic review and meta-analysis. Cancers. 2021 Mar 17;13(6):1348. https://doi.org/10.3390/cancers13061348

[16] Rallis KS, Kleeman SO, Grant M, Ordidge KL, Sahdev A, Powles T. Radiomics for renal cell carcinoma: Predicting outcomes from immunotherapy and targeted therapies A narrative review. European Urology Focus. 2021 Jul 1;7(4):717-21. https://doi.org/10.1016/j.euf.2021.04.024

[17] Ferro M, Crocetto F, Barone B, Del Giudice F, Maggi M, Lucarelli G, Busetto GM, Autorino R, Marchioni M, Cantiello F, Crocerossa F. Artificial intelligence and radiomics in evaluation of kidney lesions: a comprehensive literature review. Therapeutic Advances in Urology. 2023 Apr;15:17562872231164803. https://doi.org/10.1177/17562872231164803

[18] Salu P, Reindl KM. Advancements in circulating tumor cell research: bridging biology and clinical applications. Cancers. 2024 Mar 20;16(6):1213. https://doi.org/10.3390/cancers16061213

[19] Xing J, Liu Y, Wang Z, Xu A, Su S, Shen S, Wang Z. Incremental value of radiomics with machine learning to the existing prognostic models for predicting outcome in renal cell carcinoma. Frontiers in Oncology. 2023 Apr 28;13:1036734. doi: 10.3389/fonc.2023.1036734

[20] Salimi M, Hajikarimloo B, Vadipour P, Abdolizadeh A, Fayedeh F, Seifi S. Non-invasive prediction of nuclear grade in renal cell carcinoma using CT-Based radiomics: a systematic review and meta-analysis. Abdominal Radiology. 2025 Jun 11:1-20. DOI https://doi.org/10.1007/s00261-025-05056-x

[21] Oh CH, Kim HJ. Spontaneous Dramatic Regression of Clear Cell Renal Cell Carcinoma After Pazopanib-Induced Severe Systemic Inflammatory Syndrome: A Case Report and Literature Review. Current Oncology. 2025 Apr 30;32(5):260. https://doi.org/10.3390/curroncol32050260

[22] Tabei A, Watanabe M, Ikeuchi H, Nakasatomi M, Sakairi T, Kaneko Y, Maeshima A, Kaira K, Hirato J, Nojima Y, Hiromura K. The analysis of renal infiltrating cells in acute tubulointerstitial nephritis induced by anti-PD-1 antibodies: a case report and review of the literature. Internal Medicine. 2018 Nov 1;57(21):3135-9. https://doi.org/10.2169/internalmedicine.0444-17

[23] Cortazar FB, Kibbelaar ZA, Glezerman IG, Abudayyeh A, Mamlouk O, Motwani SS, Murakami N, Herrmann SM, Manohar S, Shirali AC, Kitchlu A. Clinical features and outcomes of immune checkpoint inhibitor–associated AKI: a multicenter study. Journal of the American Society of Nephrology. 2020 Feb 1;31(2):435-46. *DOI:* 10.1681/ASN.2019070676

[24] Xu L, Wang D, Wu Y, Zhang C, Miao P. Immunotherapy combined with chemotherapy in neoadjuvant therapy for locally advanced renal pelvis carcinoma: A case report and literature review. IJS Oncology. 2022 Jan 1;7(1):68-74. *DOI:* 10.29337/ijsonco.141

[25] Gowda S, Mathew P. Systemic Therapies for the Treatment of Renal Cell Carcinoma. InRenal Cancer: Contemporary Management 2025 Oct 1 (pp. 435-446). Cham: Springer Nature Switzerland. DOI https://doi.org/10.1007/978-3-031-97599-8_22

[26] Takeda M, Akamatsu S, Kita Y, Goto T, Kobayashi T. The Roles of Extracellular Vesicles in the Progression of Renal Cell Carcinoma and Their Potential for Future Clinical Application. Nanomaterials. 2023 May 11;13(10):1611. https://doi.org/10.3390/nano13101611

[27] Silverman SG, Pedrosa I, Ellis JH, Hindman NM, Schieda N, Smith AD, Remer EM, Shinagare AB, Curci NE, Raman SS, Wells SA. Bosniak classification of cystic renal masses, version 2019:

an update proposal and needs assessment. Radiology. 2019 Aug;292(2):475-88. https://doi.org/10.1148/radiol.2019182646

[28] Remer EM. Mimics and pitfalls in renal imaging. Radiologic Clinics. 2020 Sep 1;58(5):885-96. 10.1016/j.rcl.2020.05.001

[29] Mayerhoefer ME, Materka A, Langs G, Häggström I, Szczypiński P, Gibbs P, Cook G. Introduction to radiomics. Journal of Nuclear Medicine. 2020 Apr 1;61(4):488-95. DOI: https://doi.org/10.2967/jnumed.118.222893

[30] Zhu M, Gu Z, Chen F, Chen X, Wang Y, Zhao G. Application of artificial intelligence in the diagnosis and treatment of urinary tumors. Frontiers in Oncology. 2024 Aug 12;14:1440626. doi: 10.3389/fonc.2024.1440626

[31] Urmantsev MF, Tavabilov RI, Bakeev MR. Genetic Variation and Metabolic Basis of Kidney Cancer: New Opportunities for Targeted Therapy. SURGERY and. 2024;14(3). DOI: 10.24060/2076-3093-2024-14-3-264-274

[32] Choi JW, Hu R, Zhao Y, Purkayastha S, Wu J, McGirr AJ, Stavropoulos SW, Silva AC, Soulen MC, Palmer MB, Zhang PJ. Preoperative prediction of the stage, size, grade, and necrosis score in clear cell renal cell carcinoma using MRI-based radiomics. Abdominal Radiology. 2021 Jun;46(6):2656-64. DOIhttps://doi.org/10.1007/s00261-020-02876-x

[33] Klatte T, Rossi SH, Stewart GD. Prognostic factors and prognostic models for renal cell carcinoma: a literature review. World journal of urology. 2018 Dec;36(12):1943-52. DOIhttps://doi.org/10.1007/s00345-018-2309-4

[34] Pandolfo SD, Wu Z, Campi R, Bertolo R, Amparore D, Mari A, Verze P, Manfredi C, Franco A, Ditonno F, Cerrato C. Outcomes and techniques of robotic-assisted partial nephrectomy (RAPN) for renal hilar masses: a comprehensive systematic review. Cancers. 2024 Feb 6;16(4):693. https://doi.org/10.3390/cancers16040693

[35] Khorasanchi A, Goodstein T, Dason S, Singer EA, Zimmerman D, Yang Y. Perioperative systemic therapy in high-risk renal cell carcinoma following nephrectomy: a narrative review. Translational Cancer Research. 2024 Jun 25;13(11):6511. doi: 10.21037/tcr-24-16

[36] Ricketts CJ, De Cubas AA, Fan H, Smith CC, Lang M, Reznik E, Bowlby R, Gibb EA, Akbani R, Beroukhim R, Bottaro DP. The cancer genome atlas comprehensive molecular characterization of renal cell carcinoma. Cell reports. 2018 Apr 3;23(1):313-26. DOI: 10.1016/j.celrep.2018.03.075

[37] Paner GP, Stadler WM, Hansel DE, Montironi R, Lin DW, Amin MB. Updates in the eighth edition of the tumor-node-metastasis staging classification for urologic cancers. European urology. 2018 Apr 1;73(4):560-9. https://doi.org/10.1016/j.eururo.2017.12.018

[38] Takemura K, Navani V, Heng DY, Ernst MS. Prognostic factors in advanced renal cell carcinoma. InIntegrating Multidisciplinary Treatment for Advanced Renal Cell Carcinoma 2023 Nov 2 (pp. 233-250). Cham: Springer International Publishing. DOI https://doi.org/10.1007/978-3-031-40901-1_10

[39] Alam R, Patel HD, Osumah T, Srivastava A, Gorin MA, Johnson MH, Trock BJ, Chang P, Wagner AA, McKiernan JM, Allaf ME. Comparative effectiveness of management options for patients with small renal masses: a prospective cohort study. BJU international. 2019 Jan;123(1):42-50. **https://doi.org/10.1111/bju.14490**

[40] Chaudhary K, Pareek T, Devana SK, Sharma AP. Biomarkers in Renal Cell Carcinoma. InMolecular Biomarkers for Cancer Diagnosis and Therapy 2024 Jun 30 (pp. 483-492). Singapore: Springer Nature Singapore. DOI https://doi.org/10.1007/978-981-99-3746-2_23

[41] Linehan WM, Schmidt LS, Crooks DR, Wei D, Srinivasan R, Lang M, Ricketts CJ. The metabolic basis of kidney cancer. Cancer discovery. 2019 Aug 1;9(8):1006-21. https://doi.org/10.1158/2159-8290.CD-18-1354

[42] Chenam A, Lau C. Management of small renal masses. Genitourinary Cancers. 2018 Sep 1:105-26. DOIhttps://doi.org/10.1007/978-3-319-93339-9_5

[43] Correa AF, Jegede OA, Haas NB, Flaherty KT, Pins MR, Adeniran A, Messing EM, Manola J, Wood CG, Kane CJ, Jewett MA. Predicting disease recurrence, early progression, and overall survival following surgical resection for high-risk localized and locally advanced renal cell carcinoma. European urology. 2021 Jul 1;80(1):20-31. https://doi.org/10.1016/j.eururo.2021.02.025

[44] Mir MC, Capitanio U, Bertolo R, Ouzaid I, Salagierski M, Kriegmair M, Volpe A, Jewett MA, Kutikov A, Pierorazio PM. Role of active surveillance for localized small renal masses. European urology oncology. 2018 Aug 1;1(3):177-87.https://doi.org/10.1016/j.euo.2018.05.001

[45] Ward RD, Tanaka H, Campbell SC, Remer EM. 2017 AUA renal mass and localized renal cancer guidelines: imaging implications. Radiographics. 2018 Nov;38(7):2021-33. https://doi.org/10.1148/rg.2018180127