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Using Artificial Intelligence to Advance Renal Cancer Diagnosis, Treatment, and Precision Medicine

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Abstract

Renal cancer (RC) ranks tenth among the most frequently diagnosed cancers and affects both men and women worldwide. This disease is a significant global health issue, highlighting the need for accurate and rapid diagnostic tools to guide treatment. Conventional pathological methods have drawbacks, such as extended evaluation procedures and inter-observer inconsistency. Recent developments in artificial intelligence (AI) have enabled the progress of AI-powered computer-assisted diagnostic and predictive systems for various diseases, including cancer. A comprehensive literature review examined the latest advancements in AI and RC technologies. Advanced image analysis methods enable AI systems to measure molecular and cellular markers, thereby improving the precision and reproducibility of RC detection. This narrative review highlights the basic ideas and comprehensively summarizes modern AI methods for RC. Early clinical outcome prediction, renal carcinoma subtyping, grading, staging, and disease identification are only areas in which their potential has been demonstrated. Before applying this in daily practice, healthcare practitioners must understand the fundamentals and interact across different fields to standardize datasets, establish relevant outcomes, and merge interpretations.

Key words renal cancer, artificial intelligence, machine learning, deep learning, treatment

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Introduction

RC is an aggressive tumor that originates in the epithelial lining of the renal tubule. It is the tenth most prevalent cancer in men and women globally [1]. The incidence of RC has increased significantly. In the United States, approximately 81,800 new cases of RC are anticipated in 2023, with an estimated 14,890 fatalities [2]. RC comprises diverse tumors characterized by varying histological features, molecular profiles, clinical outcomes, and treatment responses [3]. The predominant types include clear cell renal cell carcinoma (ccRCC), papillary renal cell carcinoma (pRCC), and chromophobe renal cell carcinoma (chRCC) (**Figure 1**) [4]. ccRCC is the predominant subtype, accounting for 70%-80% of cases, and is assessed using the World Health Organization/International Society of Urology (WHO/ISUP) grading system [5]. Angiomyolipomas and oncocytomas are significant benign lesions in 0.4%, 3.0%, and 7.0% of solid renal tumors, respectively [6]. Although there have been improvements in the understanding of the molecular biology of RC and the development of more effective medicines, a wide range of therapeutic needs remains unaddressed, and significant knowledge gaps persist.

AI has transformed medical research and clinical practice, significantly improving the diagnosis, management, and prevention of various cancers [7-9]. Advanced AI techniques, including deep learning (DL), machine learning (ML) [10], and natural language processing, and offer considerable promise for enhancing research in the field of RC [11]. These technologies employ extensive and varied datasets, including radiological images, genomic data, histopathological results, and clinical records, to facilitate early detection, prognostic evaluation, treatment planning, and monitoring of therapeutic outcomes [12, 13]. The primary factors that lead to kidney carcinoma are illustrated in **Figure 2**.

In recent years, several promising studies have been published on using AI for treating RC and other urologic tumors. Several analyses have been performed to summarize and evaluate the role of AI in RC; however, there is a scarcity of comprehensive systematic assessments specifically addressing AI-related studies in RC [14, 15]. Our primary objective in writing this narrative review is to focus solely on AI and its role in RC, providing medical professionals and researchers with valuable information with the ultimate aim of advancing patient outcomes and updating the RC intervention standards.

Analysis criteria

An electronic repository and search application were employed to comprehensively evaluate the peer-reviewed literature, including original research related to experimental and qualitative research, case study collections, and other relevant publications. Key databases such as PubMed, Google Scholar, Scopus, Web of Science, bioRxiv, medRxiv, CNKI, and WanFang Data are the major information systems used in medical studies. The search was conducted between January 2017 and January 2025 using the following keywords either separately or in combination: "Renal Tumors", "Kidney Cancer", "Renal cancer", "Renal Cell carcinoma", "Clear Cell RCC", "Non-Clear Cell RCC", "papillary renal cell carcinoma", "Artificial Intelligence", "Machine Learning", and "Deep Learning". To illustrate the current landscape of AI in renal cancer, we selected 70 high-yield articles for this narrative review.

Artificial intelligence

AI is a research domain that creates computer systems that mimic human intellectual capabilities [16]. Complex computer technologies are used to perform activities that typically require human intelligence. These activities involve observing, discovering patterns, making decisions, and solving problems at or above human levels [17]. AI aims to create a machine that can accurately interpret its environment and undertake actions that enhance the probability of achieving success [18]. In medicine, AI utilizes complex algorithms, such as ML and DL, to evaluate sophisticated medical records, facilitate diagnostic evaluation and therapeutic strategies, and improve treatment efficacy [19, 20]. ML methods consist of algorithms that utilize input data to generate predictions, classifying them into the more general category of AI [21, 22]. DL represents a specialized approach within the field of ML that emerged from the progressive development of artificial neural networks [23, 24]. AI is transforming multiple medical fields and can address significant challenges in oncology, ultimately improving the accessibility and standards of cancer care worldwide.

Initially, AI platforms depended on rule-based thinking performed by computer systems in accordance with a set of steps and protocols developed by human specialists [25]. However, these systems are deficient in the cognitive capabilities necessary for handling "exceptional cases" that are not explicitly specified within the knowledge base [26]. Over the past decade, algorithms that facilitate the automation of image-based processes have evolved significantly. This transition has been marked by the resurgence of neural networks, an ML algorithm based on understanding human brain function.

Data is the primary requirement for all algorithms. This includes not only baseline patient details (e.g., age or comorbidities) but also data obtained during surgical procedures, such as surgical footage, staff engagement, and intraperitoneal pressure [27]. Owing to the accessibility of larger datasets, advances in algorithm development, and improvements in computing capabilities, there has been a surge in interest in this field of study, leading to the development of new "deeper" neural networks [28]. Using training data, algorithms can automatically learn the map of 'hidden neurons' connecting the input and output nodes without reasoning rules. DL algorithms exhibit a superior learning capacity to earlier AI models, effectively identifying complex, non-linear relationships within datasets. Therefore, DL has the potential to gradually resemble or even surpass human capabilities for highly complicated tasks and has been used in several healthcare settings [29].

Artificial intelligence and digital pathology in cancer care

Digital pathology (DP) enhances conventional pathological techniques and specializations [30]. It plays a vital role in clinical practice and has become a technological necessity in scientific laboratories [31, 32]. DP employs advanced technology and computer-augmented instruments to transform visual representations from conventional microscope slides into high-definition digital images [33].

Over the past two decades, whole-slide images (WSIs) have progressed significantly, facilitating DP and high-quality slide storage [34]. WSI is a technology that facilitates the creation and viewing of high-quality digital images of microscopic slides on computer screens [35].

Initially, DP was defined to encompass the digital capture of WSIs using sophisticated slide-scanning methods. Its definition has since broadened to include the application of AI techniques for the detection, segmentation, diagnosis, and analysis of computerized images (**Figure 3**) [36]. To the best of our knowledge, Mukhopadhyay et al. conducted the first large-scale, multidisciplinary evaluation of the diagnostic accuracy of DP and traditional microscopy. The study consisted of samples from 1,992 patients with distinct tumor classifications, and 16

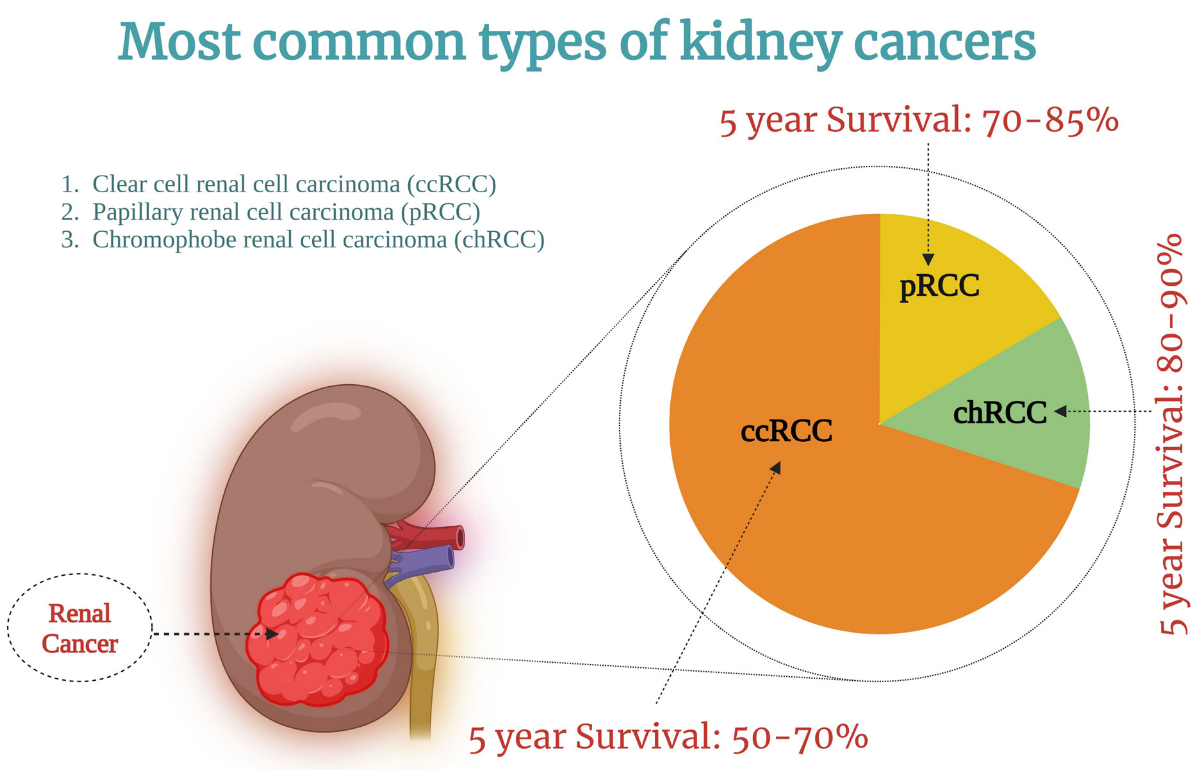

Figure 1. Illustration of various forms of renal cancer along with their associated survival rates.

surgical pathologists collaborated on the study. The outcome of this research suggests that the primary diagnostic effectiveness of WSIs is not inferior to that of traditional microscopy-based methods, with a significant variation rate from the normal range of 4.9% for WSIs and 4.6% for microscopy [37]. The comprehensive data offered by WSIs, in conjunction with other data modalities, enhances ML models in healthcare settings, resulting in improved accuracy and facilitating individualized healthcare [38].

The integration of WSI and AI holds significant promise for oncology and precision medicine [39]. This emerging innovation holds promise for transforming cancer diagnostic processes [40]. It offers advantages such as image and data sharing, improved productivity, and integrated diagnosis. Moreover, it streamlines the processes within pathology workflows, elevates the quality of patient care, encourages collaborative efforts, strengthens physician responsibility, and reduces expenses by enhancing staff efficiency [41]. The combined use of DP and AI technologies can potentially improve cancer care by integrating quantitative tissue analysis with subjective assessments by experienced pathologists. Utilizing digital imaging and AI can provide deeper insights into cancer characteristics, leading to more focused and effective treatment methods. However, the pathway to this vision is not without its difficulties or challenges. **Table 1** outlines the limitations of AI use in DP.

Artificial intelligence in renal cancer (RC)

In recent years, AI has revolutionized the field of RC diagnostics by introducing innovative approaches that enhance the accuracy and efficiency of cancer detection and diagnosis in patients with RC [54]. RC is a significant global health concern, with elevated prevalence and fatality rates. Accurate diagnosis and prognostic assessment are crucial for enhancing overall survival (OS) and updating management approaches [55]. The processes of classification, staging, and grading are intrinsically reliant on morphological data, which play a pivotal role in assessing patient prognosis [56]. Although AI has made significant strides, inconsistencies in observer evaluations and extended analysis duration remain prevalent.

Utilizing AI for the early detection of renal malignancy

Renal cell biopsy is regarded as the definitive method for diagnosing renal cancer before definitive treatment; however, imaging characteristics observed through CT and MRI also play a crucial role. The integration of AI in the early detection of RC has the potential to improve outcomes by facilitating timely diagnosis. It aims to enhance the non-invasive characterization of kidney tumors. The study looked at how to describe kidney tumours using CT imaging, mainly using radiomic features like texture and intensity from multi-stage CT-based images (preliminary contrast, corticomedullary junction, nephrographic, and, less often, excretory phase) [57, 58]. They used an ML classifier to differentiate between non-cancerous and cancerous pathologies or to group different subtypes [59]. Models aimed at differentiating benign from malignant kidney tumours have primarily concentrated on separating fat-poor angiomyolipoma's from RC. These models have demonstrated excellent outcomes, with area under the receiver operating characteristic curve (AUC) performance metrics ranging from 0.9029 [60] to 0.96 [61, 62].

Erdim et al. analyzed the differentiation of oncocytomas and fat-poor angiomyolipoma's from all RC, achieving a favorable AUC of 0.91 [63]. Efforts to differentiate ccRCC from non-ccRCC have consistently achieved high AUC values of 0.91 [64], 0.93 [65], and 0.95 [66], respectively. However, distinguishing chrRCC from non-chrRCCs remains difficult, as evidenced by an AUC of 0.82. Han et al. observed a significant decline in performance when utilizing advanced DL techniques to classify three distinct RC subtypes: ccRCC, pRCC, and chrRCC, achieving an accuracy of 73%. This performance is notably lower than the 85% accuracy obtained in the binary classification task of distinguishing ccRCC from non-ccRCC [67].

The utilization of MRI, with its multiple sequences for the detailed characterization of a renal mass, introduces a considerable challenge in the realm of AI algorithm development [68]. This challenge stems from the need to create and train algorithms that can effectively process the expanded dataset and accommodate the variability in noise and signals across various scans [69]. Xi et al. recently highlighted the enhanced accuracy of a composite model utilizing a DL ResNet framework. This model, which integrates pre-surgical T2-weighted and T1-after contrast MRI series with clinical parameters such as gender, age group, and lesion mass, was evaluated against an imaging-based model and expert analysis for differentiating benign from cancerous renal lesions in a sample of 1,162 patients. Despite the model's innovative design, its reported overall accuracy of 70% (95% CI, 60%–77%), sensitivity of 92% (95% CI, 82%–97%), and specificity of 41% (95% CI, 28%–55%) indicate a pressing need for further refinement to enhance the AI model performance for broader clinical use [70].

Utilizing AI for the grading of renal cancer

Grading is crucial for estimating the prognosis of RC patients. Similar to distinguishing between indolent and aggressive RC subtypes, differentiating low-grade RCs from their more aggressive high-grade forms is essential for developing effective clinical management strategies. Despite being primarily replaced by the WHO/ISUP grading classification system, the Fuhrman grading system remains a significant independent prognostic tool, associated with an increased risk of cancer recurrence and a reduced likelihood of patient survival [71, 72]. The Fuhrman grading system is primarily concerned with nuclear morphology, focusing on the size and shape of the nucleus and the presence of prominent nucleoli. Nonetheless, it is essential to note that there is considerable variability between different observers and within the same observer over time [73].

Chen et al. presented a model termed Retrieval with Clustering-guided Contrastive Learning (RetCCL), which employs weak supervision to classify high-grade Fuhrman predictions [74]. In a related study, Zhen et al. presented the Self-Supervised Learning based Clustering-constrained Attention Multiple Instance Learning (SSL-CLAM) model. This innovative AI model, grounded in self-supervised learning, showed improved efficacy when used in conjunction with pathologists' diagnostic assessments [75]. Although the Fuhrman grading system is valued for its practical application, its reliability is diminished because of evaluation inconsistencies among observers [76]. In response to these constraints, researchers affiliated with the ISUP and WHO developed a grading framework that classifies tumors into four distinct levels (1 to 4), determined by the degree of nucleoli

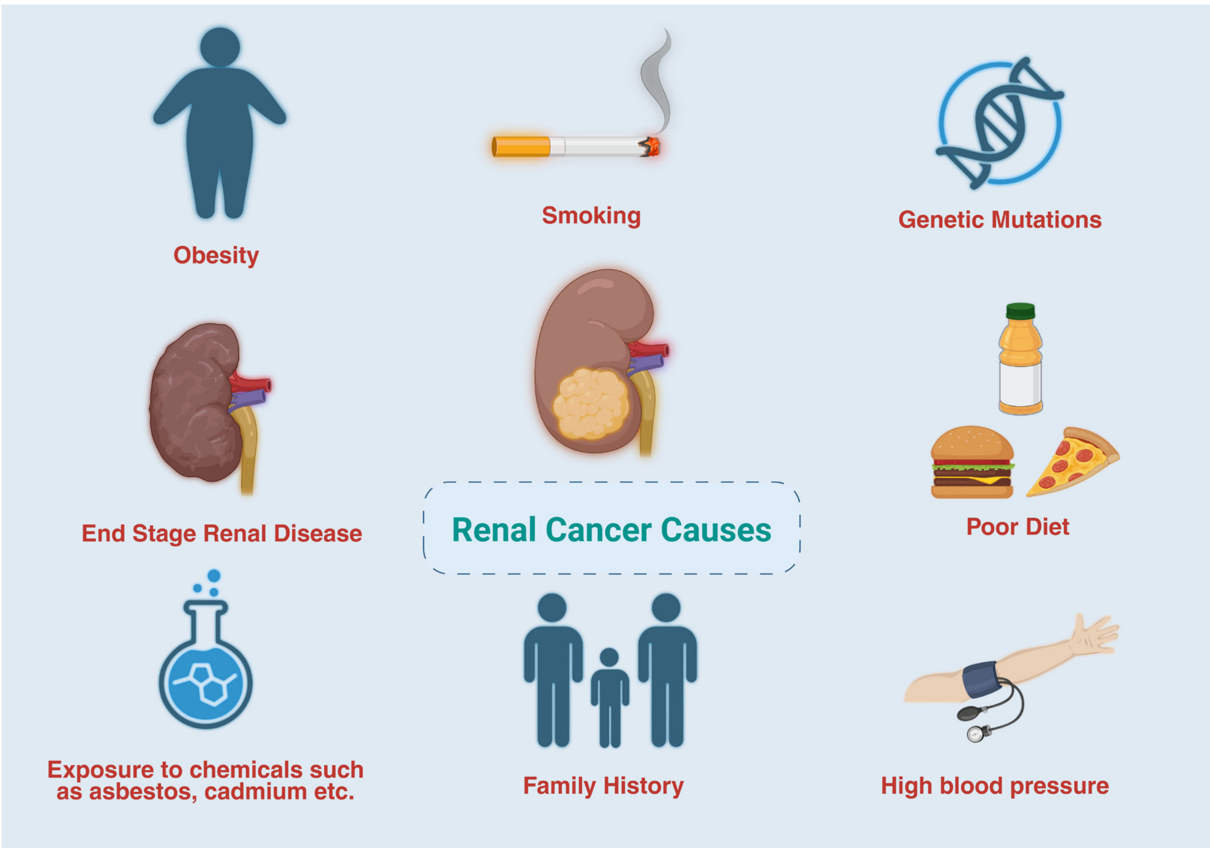

Figure 2. The principal factors contributing to kidney cancer are presented.

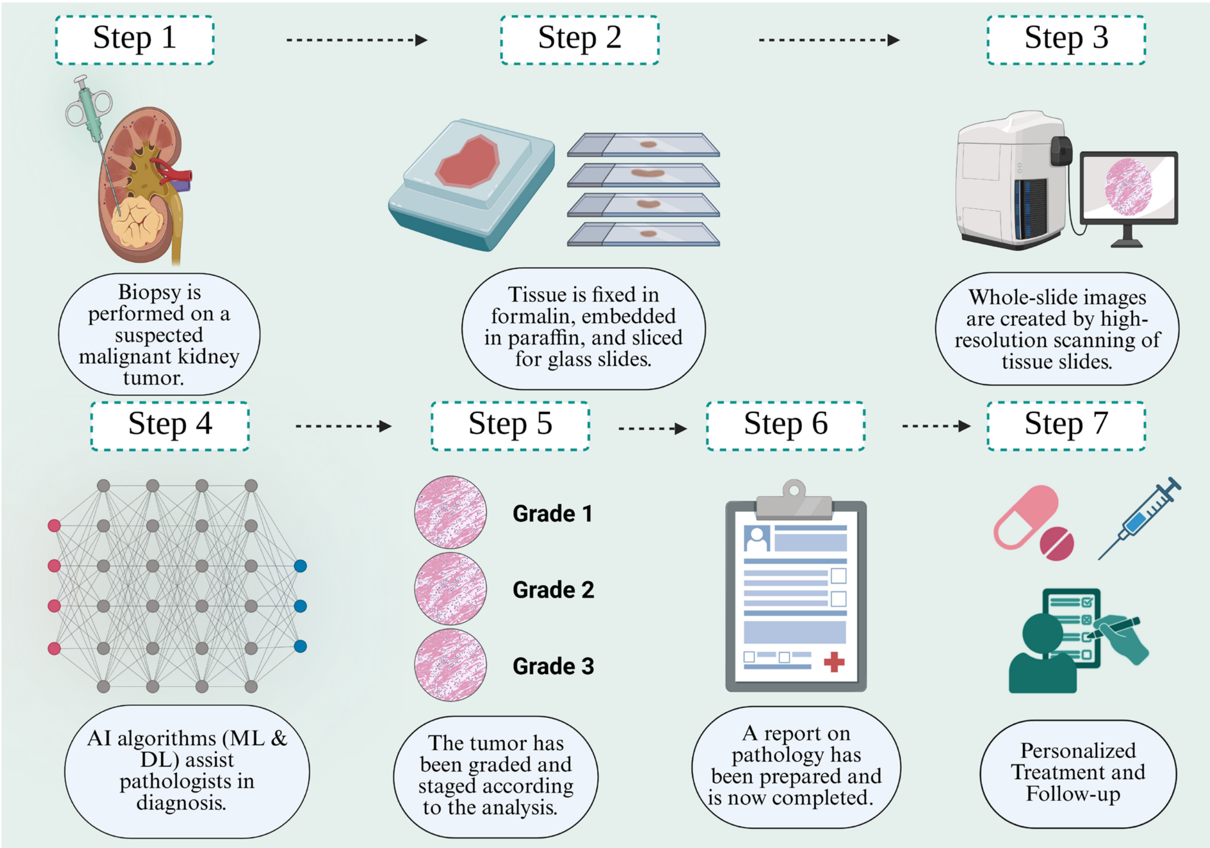

Figure 3. A comprehensive series of steps for DP in treating RC encompasses the procedure from biopsy to the outcome.

visibility [77]. Aziz et al. advanced the field by developing a ResNet-50-based attention based model that integrates patch release interpretations with center-based loss, thereby exceeding the performance of current innovative RC-grading models [78]. Koo et al. adopted a combination strategy that leveraged well-established layouts to enhance the accuracy of cancer diagnosis [79]. Chanchal et al. introduced the RCC Grading Network (RCCGNet), which demonstrated superior accuracy compared with traditional models [80].

Recent research has explored the application of AI to assess indirect measures of tumor behavior, particularly the SSIGN score, which evaluates stage, dimensions, severity level, and necrosis to predict ccRCC progression following radical nephrectomy [81]. Choi et al. conducted a study on an AI algorithm designed to preoperatively predict SSIGN scores, differentiating between low and high scores, in patients diagnosed with ccRCC who were to undergo MRI before surgery. The algorithm achieved a notable AUC of 0.94, indicating a high predictive accuracy [82].

Utilizing AI for the staging and prognosis assessment

RC staging plays a pivotal role in shaping therapeutic approaches and anticipating prognostic outcomes [83-85]. As the dimensions and positioning of cancer are pivotal in determining its stage, AI has demonstrated promise in delivering precise and uniform categorization of cancer. Yao et al. utilized the MIL approach to categorize RCC stages 1–4, resulting in a precision rate of 0.8 [86]. Survival risk estimation and analysis is a dynamic and expanding area of study. Beyond traditional statistical approaches like the Cox proportional hazards regression analysis model, the field is witnessing continuous and noteworthy developments [87, 88]. AI utilizes extensive clinical data, genomic data, and tomography datasets to estimate overall, progression-free, and recurrence-free survival accurately. These models support the automated extraction of features from data characterized by high dimensionality, thereby facilitating the discovery of new risk factors and prognostic indicators. Gao et al. focused on predicting lymph node tumor dissemination [89]; however, Liu et al. examined tumor mutation rate classification, reflecting a shift in therapeutic and research directions for RC [90]. Although staging classification shows significant potential, research in this area is comparatively limited when evaluated against studies on subtype classification and grading. The system complexity of creating a thorough analysis necessary for precise staging is partially responsible for this limitation. Moreover, the use of AI in RC research is still gaining momentum, contributing to the limited number of studies in this area.

Conclusion

AI is increasingly employed as a diagnostic and prognostic instrument in RC; however, the lack of extensive data presents a significant challenge for developing high-performing AI models. Facilitating collaboration among various centers is crucial for analyzing statistics inadequacies. For example, developing multi-center networks in RC analysis can facilitate the acquisition of varied datasets, enhance the robustness of external assessments, and ensure the effectiveness of AI models function effectively in RC clinical settings. Additionally, subsequent research could benefit from the integration of multimodal strategies.

Table 1. Overview of the limitations associated with AI implementation in DP.

Factors	Explanation	References
Clarity and consistency	The challenges these factors pose in AI models prevent the vast potential of utilizing these methods for complicated tasks. The scientific community is increasingly adopting a model emphasizing transparency, open access, and consistency methodologies.	[42, 43]
Task specificity	The term "task specificity" describes an AI's ability to excel at a single activity; for example, determining the subtypes of cancer in an organ using histology slides. A modification in the number of grades, organ type, or cancer type (within the same organ) will compromise the model's effectiveness, leading to a notable decline in its reliability and accuracy, resulting in a redesign of the model.	[44, 45]
Interpretability	One of the problems of using DP and AI together is that they are difficult to understand, which is sometimes called "black box" features. The process of making choices often lacks transparency, making it confronting for pathologists to realize the logic behind a specific diagnosis.	[46-48]
Algorithm errors	AI models for DP must be trained on substantial histological image databases with pathological classifications and data from clinical trials. Factors such as inadequate representation of target populations, imaging accuracy, or technological deviations can provide incorrect results in clinical settings when using such models.	[49-51]
Legislative and verification challenges	Due to the rapid progress of DP and AI applications, comprehensive regulatory supervision is needed to ensure patient safety and practical application in clinical settings. Regulatory bodies, including the FDA and the European Medicines Agency, have drafted guidelines to evaluate and approve DP systems and other AI-driven healthcare technologies.	[52, 53]

In conclusion, ongoing research is dedicated to evaluating the roles of CT and MRI in diagnosing RC and forecasting clinical outcomes and therapeutic responses to optimize management strategies. The improvements in the timely detection of RC and the anticipation of treatment outcomes largely depend on recognizing ideal discriminative indicators tailored to specific diagnostic and predictive challenges. This progress is further supported by creating robust, consistent, and versatile AI-based diagnostic and predictive models. By outlining these future initiatives and recommendations, we seek to motivate researchers and investors to close this knowledge gap and realize the objective of developing an integrated system. This system should be reliably utilized for diagnosing renal tumors and predicting clinical outcomes and treatment responses, eventually contributing to advances in health care outcomes.

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Ethical policy

Non applicable.

Availability of data and materials

All data generated or analysed during this study are included in this publication.

Author contributions

Darragh Walsh contributed to design of the work, data collection, and drafting the article; Callum Hayes checked the revision manuscript and approved the final submission.

Competing interests

The author declares no competing interests.

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