Yemen Journal of Medicine

https://yemenjmed.com

Article information

DOI: 10.63475/yjm.v4i2.0113

Article history:
Received: 20 May 2025
Accepted: 10 June 2025
Published: 22 September 2025

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How to cite this article
Habas E, Rayani A, Abograra A, Habas E, Allagi B, Habas A, et al. Renal mass: Epidemiology, clinical presentation, diagnostic strategies, management, and outcomes: A comprehensive update. Yemen J Med.2025;4(2):214-237

Review Article

Renal Mass: Epidemiology, Clinical Presentation, Diagnostic Strategies, Management, and Outcomes: A Comprehensive Update

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ABSTRACT

Kidney mass lesions are common and are often discovered accidentally. Renal cell carcinoma (RCC) represents approximately 5% of all cancers. Men have a two-fold higher likelihood of developing the disease and experience a higher mortality rate than females. The differences between the genders are attributed to individual variations, including hereditary factors, underlying medical conditions, genetics, lifestyle, hormonal factors, and others, such as hypertension and obesity. Renal tumors are usually asymptomatic; however, hematuria, dull aching flank pain, and lower abdomen pain can present symptoms. A tissue biopsy is typically unnecessary but may be required in certain cases. Men tend to exhibit larger and more severe tumors. Radiology tools application is helpful for early diagnosis and follow-up. Partial or radial nephrectomy is an effective curative therapy in localized renal masses. Nevertheless, immunotherapy, cryotherapy, and sometimes chemotherapy are used, especially in high-income nations. In this review, epidemiology, pathophysiology, risk factors, presentation, diagnosis, and kidney mass management will be reviewed and updated. Different keywords and phrases, such as kidney malignancy, renal cancer, epidemiology of kidney cancer, nephrectomy in kidney masses, and management of renal cell tumors, were used to search PubMed, EMBASE, Scopus, Google, and Google Scholar for new reviews and original articles and new comments with updates that were published between January 2019 and May 2025.

Key words: Kidney cancer, renal cell carcinoma, RCC prevalence, renal cancer stages, risk factors, RCC outcomes

INTRODUCTION

Kidney masses are common; they are usually asymptomatic and discovered accidentally. In the old population, kidney cancer ranks as the 6th in men and the 10th in females globally, accounting for 5% and 3% of all new cases, respectively. [1] Renal cell carcinoma (RCC) is a heterogeneous group of molecular and histopathological tumors. The recent advancement in understanding RCC morphology, genomics, immunohistochemistry, and epidemiology has led to the recognition of novel features in RCC molecular pathological epidemiology. [2] Based on these discovered features, the RCC classification was revised in 2016. [3] The most common subtypes of RCC are clear cell (CC; 65%–70%), papillary RCC

(PRCC; 15%–20%), and chromophobe (5%–7%). [2] RCCs primarily occur in the renal cortex, accounting for 80% to 85% of primary renal malignancies. Tumors such as transitional cell carcinomas of the renal pelvis account for about 8% of cases. Other rare kidney epithelial tumors in the parenchyma include oncocytomas, angiomyolipoma (AMLP), collecting duct tumors, and renal sarcomas. [4] It is estimated that > 4,600 people were diagnosed with kidney cancer in 2023, and RCC accounts for about 90% of all cases in Australia. Kidney cancer is the seventh most commonly diagnosed cancer in Australia, and it is estimated that one in 65 people will be diagnosed by the time they are 85 years of age. [5] Approximately 65,000 cases of RCC are diagnosed each year in the United States. Individuals affected by the condition are usually between 50 and 70 years old. [6] One reason for the increasing incidence of kidney cancer diagnoses may be that imaging techniques, such as computerized tomography (CT) scans, are being used more frequently. These investigations have led to the accidental discovery of more kidney cancers. It was reported that RCC is confined to the kidney in 45%, is locally invasive in around 33%, and has spread beyond the kidney to other organs in approximately 25% of cases at presentation. [6] Other less common types include urothelial carcinoma (also known as transitional cell carcinoma), which can originate in the renal pelvis. Wilms' tumor is most common in younger children, although it is still rare. A renal mass or tumor can be associated with hereditary diseases, such as Von Hippel-Lindau (VHL) disease.

Renal tumors usually present with either incidental (asymptomatic) findings (60%–70%) or symptomatic (local or systemic) presentations (30%–40%). The Classic Triad typically occurs in late-stage cases, affecting fewer than 10%. The triad consists of flank pain (40%), hematuria (50%), and a palpable mass (30%). Hypercalcemia is due to paraneoplastic effects or bone metastasis. A complete blood count, serum alkaline phosphatase, kidney and renal function tests, chest X-ray, abdominal ultrasound, CT scan, and magnetic resonance imaging (MRI) must be conducted individually. According to the stage of the kidney tumor at presentation, therapy is usually planned. In this review, epidemiology, pathophysiology, risk factors, presentation, diagnosis, and management of kidney mass will be reviewed and updated.

RENAL CELL TUMOR CLASSIFICATION AND CHALLENGES

The 2016 World Health Organization (WHO) classification identifies over 14 subtypes of RCC, with the most clinically significant being. [7] (A) CC RCC accounts for 70% to 80% of cases. It is characterized by 3p chromosome loss (VHL gene mutations) and lipid-rich cytoplasm. [7,8] (B) pRCC represents 10% to 15% of cases; it is subdivided into Type 1 (basophilic, associated with MET mutations) and Type 2 (eosinophilic, more aggressive). [7,8] (C) Chromophobe RCC (chRCC) accounts for approximately 5% of cases. It arises from collecting duct intercalated cells with multiple chromosomal losses (1, 2, 6, 10). [7,8] (D) Collecting Duct Carcinoma and Others are rare (<1%) and include Succinate dehydrogenase (SDH)-deficient, translocation, and unclassified RCC. [8]

Renal tumor subtypes have been classified according to predominant cytoplasmic characteristics (e.g., CC and chRCC), architectural features (e.g., pRCC), anatomical location (e.g., collecting duct and renal medullary carcinomas), association with specific renal disease backgrounds (e.g., acquired cystic disease-associated RCC), and distinct molecular alterations. [9,10] CC RCC (ccRCC) is characterized by the loss of chromosome 3p and inactivation of the VHL gene, while PRCC exhibits gains on chromosomes 7 and 17. The loss of multiple chromosomes characterizes chRCC. [9]

The third edition of the World Health Organization (WHO) classification of urogenital tumors identified certain renal tumor entities based on molecular alterations in 2004. [11] However, a comprehensive molecular classification of renal tumors remains unclear. [12] In the upcoming year, extensive parallel sequencing will be increasingly utilized to identify genetic alterations in renal tumors exhibiting distinct morphology. [13] Consequently, the 2022 WHO classification incorporated molecular-driven kidney tumors alongside morphology-based tumors. [9,14]

It has been documented that morphology alone is insufficient for identifying molecularly defined kidney tumors due to their inherent heterogeneity. [9] Medullary RCC with SWI/SNF-related, matrix-associated, actin-dependent regulator of chromatin, subfamily B, member 1 (SMARCB1) deficiency, [16] RCC with alterations in transcription factor EB (TFEB), [15] RCC with ALK rearrangements, [16] and RCC with Elongin C (ELOC) mutations [17] are molecularly characterized epithelial RCCs. TFEB controls gene expression by binding to the coordinated lysosome expression and regulation (CLEAR) sequence. [18] Most ccRCC patients exhibit VHL inactivation, [13] while most metanephric tumors display B-Raf proto-oncogene, serine/threonine kinase (BRAF) p.V600E mutations, [19] indicating potential for molecular characterization. VHL wild-type ccRCC may exhibit a distinct clinical phenotype. [20] The current WHO classification represents a shift from a morphology-based system to an integrated approach incorporating numerous new "molecular entities." However, renal tumor diagnosis must be standardized to facilitate effective local, national, and international communication. A precise diagnosis necessitates a morphologic descriptive assessment utilizing light microscopy and immunohistochemistry, accompanied by a note on any molecular alterations. The fifth edition of the WHO outlines "essential and desirable diagnostic criteria" for each tumor type. Immune histological characterization (IHC), molecular biomarkers, and clinical, radiological, molecular, and histological criteria are incorporated. Innovative approaches, such as proteomics or factors related to the tumor microenvironment, may enhance this. [12] To achieve more personalized treatments, it is essential to integrate histologic diagnoses with molecular methodologies such as methylation profiling, RNA sequencing, and whole-genome and whole-exome sequencing. Therefore, pathologists and molecular experts should be included in the design teams for future clinical trials. [21] The 2022 WHO represents a significant advance but is still in the process of evolving. The emerging entities (ALK, TFEB, ELOC) have therapeutic implications. Standardization of diagnostic criteria remains crucial for both clinical care and research. Future systems will likely incorporate more comprehensive molecular profiling. **Tables 1** to **3** summarize the RCC classification.

NEW NOMENCLATURES OF RENAL TUMOR TYPES

RCC with eosinophilic solid and cystic features

Eosinophilic solid and cystic RCC (ESC RCC) exhibits distinct histological features, a Cytokeratin (CK) 20 immunohistochemical

Table 1: Classification framework for renal tumor subtypes.

Classification basis	Example subtypes	Key features	References
Cytoplasmic characteristics	Clear cell renal cell carcinoma (RCC), chromophobe RCC	Cellular appearance under microscopy	[10,11]
Architectural features	Papillary RCC (pRCC)	Growth patterns and structure	[10,11]
Anatomical location	Collecting duct carcinoma, renal medullary carcinoma	Tumor origin site	[10,11]
Disease association	Acquired cystic disease-associated RCC	Specific renal disease background	[10,11]
Molecular alterations	Various molecularly defined tumors	Genetic and epigenetic changes	[10,11]

Table 2: Molecular characteristics of major renal cell carcinoma (RCC) subtypes.

Tumor subtype	Key molecular alterations	Diagnostic significance	References
Clear cell RCC (ccRCC)	Chromosome 3p loss, Von Hippel-Lindau gene inactivation	Present in most cases (~90%)	[10,20]
Papillary RCC (pRCC)	Gains of chromosomes 7 and 17	Help distinguish from other subtypes	[10]
Chromophobe RCC	Loss of multiple chromosomes (1, 2, 6, 10, 13, 17, 21)	Better prognosis than ccRCC	[10]
Medullary RCC	SMARCB1 deficiency	Aggression is associated with the sickle cell trait	[16]
Transcription factor EB (TFEB)-altered RCC	TFEB gene rearrangements	Distinct lysosomal phenotype	[17,19]

Table 3: Recommended future directions.

Area	Current status	Needed development	Implementation challenges	References
Molecular integration	Partial (2022 WHO)	Comprehensive profiling	Standardization, cost	[13,14,16]
Clinical trial design	Traditional	Include pathologists/ molecular experts	Interdisciplinary coordination	[16]
Diagnostic reporting	Variable	Standardized templates	Global adoption	[10,13]
Therapeutic matching	Limited	Molecular-guided therapy	Validation studies	[16,18]

profile, and mutations in the tuberous sclerosis complex (TSC) gene. [22] Clinically, ESC RCC was initially characterized by indolence. [22,23] ESC RCC is associated with renal neoplasms linked to TSC gene alterations and mTOR pathway activation, which may influence patients' therapeutic options. [22]

RCC with ELOC (TCEB1) mutation

ELOC-mutated RCC (**Figure 1B**) exhibits considerable morphological variability, with ccRCC or CC PRCC being the primary differential diagnosis. Instances have been documented as tumors with angioleiomyomatous stroma. [17,24] ELOC-mutated RCCs are a model for molecularly defined subtypes, as diagnosis necessitates molecular testing. Classifying these tumors is important because they exhibit indolent behavior post-resection, although it is based on limited experience. [24]

ALK-rearranged RCC

Rare subtypes of RCC include ALK-rearranged variants. [24] This RCC exhibits extensive eosinophilic cytoplasm and significant vacuolization, demonstrating a diverse morphological range, occasionally accompanied by mucinous deposits. The diagnosis of exclusion necessitates ALK immunohistochemistry and/or fluorescence in situ hybridization before categorizing a case with an atypical combination of morphologies as "unclassified." Clinical responses of patients to targeted ALK inhibitors exhibit variability, with specific individuals demonstrating significant responses. [25]

Medullary RCC without SMARCB1

RCC in the renal medullary region encompasses collecting duct carcinoma and medullary RCC. In contrast to collecting duct carcinomas, medullary RCC exhibits a loss of SMARCB1 (INI1). [26] These neoplasms are referred to as SMARCB1-deficient medullary RCC. Individuals with young sickle cell traits frequently exhibit severe SMARCB1-deficient medullary RCC. Certain unclassified RCC instances exhibiting a medullary phenotype demonstrate complete deletion of SMARCB1, yet lack hemoglobinopathies, suggesting that sickle cell is not a prerequisite for this genetic disorder. [27] These tumors

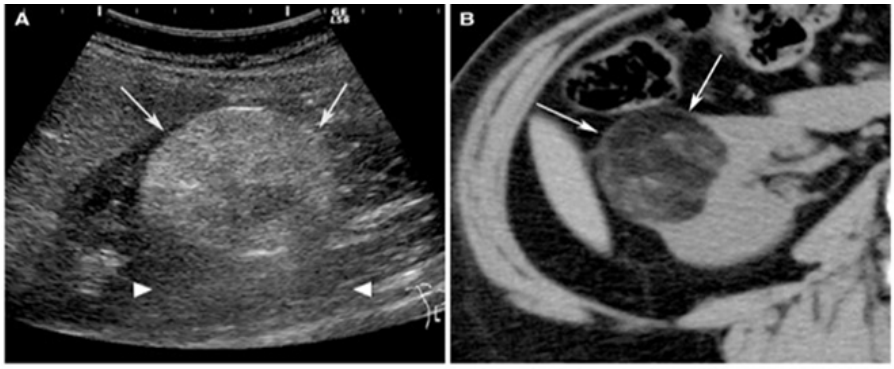

Figure 1: (A and B) Ultrasound and non-enhanced CT scan show a hyperechoic to parenchyma and fat density well-defined mass with acoustic shadow (angiolipoma).

represent subtypes of medullary RCC deficient in SMARCB1. Emerging proteasome-targeting medications suggest that molecular profiling could have significant therapeutic implications. [28] Secondary loss of SMARCB1 may be observed in other renal cancer (RC) subtypes, including ccRCC with sarcomatoid transformation, translocation RCC, or fumarate hydratase (FH)-deficient RCC. [29]

TFEB altered RCC

The fourth edition of the WHO classification of urogenital tumors categorizes TFEB translocated RCC as a microphthalmia-associated transcription factor (MiTF) translocation carcinoma. [30] Recent observations suggest that TFEB amplification and translocations contribute to establishing a new category of RCC. [15] RCCs with TFEB alterations are less common than those with transcription factor E3 (TFE3) rearrangements. While TFEB-amplified RCC is more aggressive than TFE3-translocated RCC, it is characterized by a greater degree of lethargy. [15]

(F) RCC without familial history, previously associated with hereditary leiomyomatosis and RCC (HLRCC) syndrome.

In 2016, the WHO identified RCC associated with HLRCC syndrome and FH deficiency as a distinct tumor type. [3] Investigations following the 2016 WHO categorization identified FH deficiency in "unclassified high-grade renal carcinomas," "tubulocystic carcinomas with dedifferentiated foci," "type 2 papillary carcinomas," and "collecting duct carcinomas". [31,32] Therefore, FH-deficient RCC is the appropriate designation for RCC exhibiting compatible morphology, negative FH IHC (which is highly specific but not entirely sensitive), positive 2SC IHC, and/or a pathogenic FH mutation in the tumor, mainly when the clinical and family history of skin and uterine leiomyomas is unclear. The genetic status remains undetermined. [33] HLRCC syndrome-associated RCC continues to be relevant in familial cases. Erlotinib and bevacizumab demonstrated efficacy in treating FH-deficient RCC in preliminary studies. [34] **Table 4** summarizes the RCC classification.

Table 4: Rare renal cell carcinoma subtypes and their characteristics.

Subtype	Key features	Molecular alteration	Diagnostic markers	Clinical behavior	References
Eosinophilic solid and cystic RCC (ESC RCC)	Distinct histology with eosinophilic cells and cystic spaces	TSC gene mutations	CK20+	Initially indolent	[23,24]
ELOC (TCEB1)-mutated RCC	Morphologic variability (ccRCC-like or clear cell papillary)	ELOC mutations	CK7+ (often), angioleiomyomatous stroma	Typically indolent post-resection	[13,25]
ALK-rearranged RCC	Eosinophilic cytoplasm with vacuolization, mucinous deposits	ALK rearrangements	ALK IHC/FISH	Variable	[25,26]
SMARCB1-deficient Medullary RCC	Aggressive medullary carcinoma	SMARCB1 loss	INI1−	Aggressive, young sickle cell trait patients	[27–29]
TFEB-altered RCC	- TFEB-translocated: MiTF family - TFEB-amplified: New category	TFEB alterations (translocation/ amplification)	TFEB IHC	Amplified: More aggressive Translocated: More indolent	[17,31]
FH-deficient RCC	High-grade morphology (was "unclassified")	FH mutation/ deficiency	FH- IHC, 2SC+	Aggressive	[32–36]

EPIDEMIOLOGY AND DEATH RATES OF KIDNEY MALIGNANCY

Kidney cancer comprises roughly 2% of the total number of cancer diagnoses and cancer-linked mortalities globally, with higher incidence rates often seen in industrialized nations. [35] RCC histopathological subtypes include CCRCC, reported in 75% to 85% of cases, pRCC in 10% to 15%, and chRCC in 5% to 10%, accounting for approximately 95% of RCC cases. [36,37] These subtypes exhibit unique genetic and clinical characteristics, evident in variations in metastasis, recurrence, and overall survival patterns. [38] The statistical analyses have shown CCRCC to be the most common subtype. [39,40] A comprehensive comparison is lacking; further worldwide collaborative efforts are needed.

Over the past decades, the worldwide prevalence of kidney cancer has shown different trends. Globally, the number of newly diagnosed kidney cancer cases increased from over 207,300 to 393,000 between 1990 and 2017. The age-standardized incidence rate (ASIR) increased slightly from 4.72 to 4.94 per 100,000 during the same period, despite a rise in absolute case numbers. This implies that the incidence rate changed somewhat with age while the total number of cases increased. [41,42]

Projections show that the worldwide incidence of kidney cancer could rise even further to around 475,400 by 2030. The ASIR is expected to drop somewhat to 4.46 per 100,000, though. While many developing countries are expected to continue experiencing increasing rates, the anticipated decline in incidence rates is primarily attributed to forecasted decreases in developed countries. [41]

These patterns can vary greatly depending on the area and are influenced by factors such as lifestyle changes, environmental exposures, and the availability of early detection and diagnostic tools. For example, a recent study in the United Kingdom revealed that a sizable fraction of kidney cancer cases are discovered inadvertently during unrelated medical procedures, usually at later stages, which can affect therapy outcomes and survival rates. [41]

The global incidence of RCC is approximately 403,000 new cases annually (2.2% of all cancers), with higher rates in North America and Europe (10.9/100,000). [8,43] The mortality occurs at a rate of 175,000 deaths/year (1.8% of cancer deaths). The 5-year survival rate for metastatic RCC is 12%. [7,44] There are non-modifiable and modifiable risk factors for RCs. The non-modifiable factors are gender (male predominance; 2:1 ratio) [7] and genetic syndromes (e.g., Birt-Hogg-Dube). [7] The modifiable factors include smoking, obesity, hypertension, and occupational exposure (e.g., trichloroethylene). [7,43] The incidence has doubled since 1975, mainly due to advances in imaging technology. [8,45] The mortality rates stabilized in high-income countries, primarily due to improved early detection and therapies. [43,44]

The prevalence of RCCs represents 3% of all visceral neoplasms and is the seventh most common cancer, with an increasing prevalence. [46] It is common in the sixth and seventh decades of life, with a median age of 64 years and a twofold male predominance. [47,48] Each year, around 295,000 additional cases of kidney cancer are identified globally, resulting in approximately 134,000 documented fatalities. [49,50] In 2023, the estimated number of new kidney cancer diagnoses in the United States was 81,800, constituting 4.2% of total cancer cases. Kidney cancers were predicted to cause 14,890 deaths (2.4% of cancer deaths), and the 5-year relative survival was 77.6% between 2013 and 2019. [51] Kidney cancer is responsible for around 63,000 new cases and around 14,000 fatalities per year in the United States. [52] In 2024, it is reported that the estimated number of new cases and deaths from kidney and renal pelvis cancer in the United States is 81,610 and 14,390, respectively. [51] In Europe, kidney cancer accounts for over 84,000 new cases and nearly 35,000 deaths. [53] The median age of patients diagnosed with RCC in the Surveillance, Epidemiology, and End Results (SEER) database in the United States was 64 years. When RCC is detected in individuals younger than 46 years, it corresponds to the lowest 10% of the age range. Hence, it is essential to evaluate the potential presence of an inherited kidney cancer syndrome that could be responsible for 3-5% of all RCCs. [35] Although kidney cancer development in young people has an impact on their health and socioeconomic status, there is a limited amount of extensive research that has focused on the issue of cancer prevalence among young people. [54–56] Despite these studies having notable features, there is a need for more detailed data about the occurrence rates among young people based on race, stage, and tumor characteristics. However, the institutional series [56–58] provided more specific information, albeit it did not provide data on incidence rates. [56]

Reports revealed that hereditary causes account for approximately 3% to 8% of RCC cases. [59] A single mutated gene in autosomal dominant disorders may increase susceptibility to kidney cancer. [60] The VHL gene mutation is responsible for VHL disease, a hereditary condition primarily associated with RCC. VHL disease increases the risk of CC RCC, hemangioblastomas, and pheochromocytomas. [61] Mutations in the heterozygous germline FH gene are responsible for HLRCC. [62] HLRCC is associated with aggressive PRCC, as well as cutaneous and uterine leiomyomas. BHD is associated with different kidney malignancies, including chRCC, oncocytomas, hybrid oncocytic tumors, and akin fibrofolliculomas. [63,64] Mutations in the MET gene increase susceptibility to type 1 pRCC in hereditary pRCC. [65] Regular surveillance enables individuals with a genetic predisposition to identify and address RCC at an early stage. Family counseling for hereditary syndromes facilitates genetic counseling and testing among family members, promoting informed health monitoring and interventions. Targeted therapies may be more effective in specific genetic contexts; therefore, understanding the genetics of RCC could facilitate more effective treatment selection.

The global annual incidence of kidney cancer is estimated to be 400,000 new cases, with a mortality rate of around 175,000 fatalities per year, according to another study. [66] Another study reported that RCC is the eighth most often diagnosed cancer, accounting for 4.2% of all occurrences. [56] Kidney cancer ranked 15th among newly diagnosed malignancies in 2018, causing the deaths of 403,262 persons and representing 2.2% of all cancer cases. [67] In addition, kidney cancer ranked 17th in terms of cancer-related mortality,

resulting in 175,098 fatalities, accounting for 1.8% of all cancer-associated mortalities globally. [68] The occurrence of RCC worldwide exhibits variation, with North America and the Czech Republic having the highest rates. Annually, the United States experiences over 63,000 new cases and almost 14,000 fatalities. RCC rates in the United States have been increasing since the mid-2000s. Most growth during the 1980s occurred in tumors at an early stage. [69] RCC is considered a common urinary system tumor with an increasing incidence year by year. [70,71]

In the United States alone, it was anticipated that there would be 65,340 new cases in 2018. [69] Recent research indicates North America has the most significant prevalence of RCC globally, with a cumulative risk of 1.8% in men and 0.9% in females. [72] The frequency of RCC in Saudi Arabia is consistent with regional and global statistics. The most common subtype is CC RCC, which is most often discovered incidentally, and most patients present with stage T1 disease. [12–14,16,33] An examination of local Cancer Registry data revealed a 33% increase between 1994 and 2006. [73] Additionally, research identified a 38% increase in instances of RCC from 2005–2010 to 2010–2015, with 156 cases recorded during the second period. [39] Recent research conducted from 2015 to 2023 revealed a concerning increase in the occurrence of RCC in Saudi Arabia. The incidence rate rose by around 176% compared to 2010 to 2015, with 431 cases reported as opposed to 156 instances during that time. [74]

Global cancer incidence data from 1978 to 2007 revealed a consistent female-to-male case incidence ratio of 1:2, which remained unchanged across age, year, and region. [75] Males had a comparable incidence rate from 2001 to 2016, according to an analysis of the Surveillance, Epidemiology, and End Results database; the age-adjusted incidence rate for males in the US was double that of females. [76] According to data obtained from registries on a global scale, the age-standardized incidence of kidney cancer rose by 23.04% between 1990 and 2013. This rise was 31.2% among males and 8.798% among females. [77] Moreover, this study has shown that RCC is infrequent but rising among young individuals. This was primarily attributed to the TNM staging system and the early detection of small tumors (T1aN0M0 stage); however, the prevalence has substantially increased in different regions worldwide. Variations exist among ethnic groups that may need more investigation. [56]

Worldwide, in the United States in 2025, there will be an estimated 2,041,910 new cancer cases and 618,120 cancer deaths. In 2020, the numbers were as follows: 4.6 for both sexes, 6.1 for males, and 3.2 for females. [78] Whereas, for 2013 to 2017, the Cancer Statistics Center of the American Cancer Society reported incidence rates (average annual rate/100,000, age-adjusted to the 2000 US standard population) of 16.9 for both sexes, 11.7 for females, and 22.9 for males. [79] According to data obtained in September 2021, the European Cancer Information System reported incidence rates (average annual rate/100,000, age-adjusted) for Europe in 2020 as follows: 18.4 for both sexes, 12.5 for females, and 25.9 for males. [80] Recent research has shown that the age at which RCC develops in the old population is progressively lowering, but in older people, the RCC severity and frequency rise with age. [80] The incidence of RCC may be higher in older women than in older men. Additionally, individuals aged 85 and above may have a higher risk of developing cancer, with increased rates of metastasis to lymph nodes, advanced tumor stage, and unfavorable prognosis. Therefore, older people's RCC screening should be prioritized. [80]

A study by Du et al. concluded that decreases in industrialized countries primarily drive the expected decline in RC incidence over the next decade, and more attention should be given to underdeveloped nations. [41] In 2017, Uruguay recorded the highest kidney cancer age-standardized rate (ASR) at 16.15/100,000, followed by Slovakia, Iceland, and the Czech Republic. [43] Throughout the study period, 134, 8, and 30 nations or territories experienced stable increases and encountered declines in KC ASR, respectively. [41] Armenia exhibited the most significant increase, followed by Bulgaria and Belarus. Sri Lanka exhibited the most significant decline, followed by Trinidad & Tobago and Qatar. [41]

The projected number of RC cases is expected to increase to 475.4 thousand between 2018 and 2030, with a 95% highest density interval (HDI) of 423.9. During the same timeframe, the RC ASR is projected to decrease slightly to 4.46 per 100,000. Despite the anticipated increase in case numbers, a decline is expected for both genders. From 2018 to 2030, a decline in case numbers is anticipated for individuals aged 0 to 19 years and those aged 20 to 39 years. A consistent increase is anticipated for individuals aged 40 to 64 years and those aged 65 years and older. Between 2018 and 2030, case numbers are expected to increase in all 172 countries or territories temporarily. [41]

The temporal patterns of RC ASR varied across different nations. In 2030, Uruguay is projected to have the highest kidney cancer ASR at 17.7/100,000, followed by the USA and Iceland. The United Arab Emirates is projected to experience the most significant increase, followed by Burkina Faso and Ghana. Ukraine is projected to exhibit the most significant decline, followed by Croatia and Slovakia. [41]

From 1990 to 2030, 18 to 72 nations or territories experienced a consistent decline or rise in RC ASR. Ten nations or territories experienced a historical decline and are projected to face adverse future developments. For example, it was found that after 2017, the declining trend of RC ASR in the United States will reverse. Conversely, despite previous advancements in certain regions, 61 nations or territories are projected to experience a significant decrease in RC ASR. No significant correlation was found when considering all countries collectively. Nations with a high national sociodemographic index (SDI) exhibited a significant negative correlation, indicating that most developed nations are expected to experience a favorable decline in RC ASR from 2018 to 2030. Conversely, for nations with low SDI, a significant positive correlation was observed, suggesting that most nations are likely to continue following historical trends in the future. [41]

The trend of the increase in RC might be due to the prevalence of excessive smoking and alcohol intake among these patient categories. [81,82] The observed trends may lead to an unforeseen increase in RC incidence rates globally. The incidence of US RC reversed after 2017, despite a decline, whereas the incidence of RC was anticipated to increase in

the UK and Germany while decreasing in adjacent countries. [41] The significant rise in overweight, obesity, and alcohol consumption, alongside the influx of immigrants from Africa and Asia, [83] as well as the increase among colored populations, particularly in the US, may account for this trend, potentially overshadowing the decline observed among White populations. [84] The unanticipated increase suggests that RC remains a significant health concern in highly developed nations and requires further investigation.

Following 2017, the incidence of RC diminished in most European and Australian countries, potentially contributing to the global decline. The incidence of RC has risen in Western populations over recent decades, attributed to advancements in imaging techniques that can identify small renal masses, contributing up to 50% of the overall incidence. [57,84] The observed plateau in imaging utilization and the reduction of risk factors may account for the declining trends. The incidence rate, though modest, exhibited a consistent increase in most Latin American, African, South Asian, and Southeast Asian countries from 1990 to 2017. The increase is projected to persist until 2030. Several factors may explain this increase: (A) Increasing RC detection and reporting rates. [84] (B) Expanding population, especially among the aging demographic. [85] (C) Shifting trends towards Western dietary patterns, occupational behaviors, high-risk activities (e.g., excessive caloric intake and physical inactivity), and alterations in established cancer risk factors (e.g., smoking and obesity). [85,86] (D) Increase in chronic kidney diseases, especially in nations with a high disease burden.

Clinically, the identification of kidney cancer is often fortuitous and mainly ascribed to several imaging techniques, including ultrasonography, CT, and MRI. [87] Further investigation is typically necessary to distinguish kidney cancer from non-malignant lesions. Non-malignant kidney masses include pure cysts, oncocytomas, AMLP, and small kidney masses measuring less than 4 cm, which are detectable by imaging and must be differentiated from malignant renal tumors. This is because an early and accurate diagnosis can significantly improve the prognosis of kidney cancer patients. [88] The available treatment modalities for RCC depend on the stage of the disease at the time of diagnosis. Partial nephrectomy (PNE) is the standard of care for early-diagnosed kidney-localized tumors and is linked with successful results. [89] In contrast, when RCC is at an advanced stage and has metastasized at the time of diagnosis, it is associated with a poor outcome with an increased death rate.

In summary, cc RCC dominates (75%–85%) with a distinct genetic profile. Industrialized nations exhibit a 2-3 times higher incidence than the global average. Male predominance (2:1) persists across all regions. Saudi Arabia shows the most dramatic recent increase (+176%). Projected global case increase (+21%) but ASR decline (-0.97%) by 2030. The epidemiology, risk factors, incidence trends, and treatment modalities for kidney cancer based on global data are summarized in the following **Tables 5–12**.

KIDNEY CANCER RISK FACTORS AND CAUSES

RCC's primary etiology/ies is/are complex and closely related to genetic factors, environmental factors, and living habits. [70,90] Age is a significant factor in the pathogenesis and prognosis of RCC. [70] Research has shown that the age at which RCC develops is progressively decreasing. However, in

Table 5: Global burden of kidney cancer.

Metric	1990	2017	2020	2030 (Projected)	Key observations	References
Annual new cases	207,300	393,000	403,000	475,400	2.2% of all cancers	[43,44,9]
Age-standardized incidence rate (/100k)	4.72	4.94	4.6	4.46	Declining in developed nations	[43,44,73]
Annual deaths	-	-	175,000	-	1.8% cancer deaths	[8,46]
5-year survival (metastatic)	-	-	12%	-	Improved detection helps	[8,46]

Table 6: Histopathological subtypes of RCC.

Subtype	Prevalence	Genetic features	Clinical characteristics	References
Clear cell RCC	75%–85%	VHL mutations (3p loss)	Most common, lipid-rich cytoplasm	[38–40]
Papillary RCC	10%–15%	MET mutations (Type 1)	Type 2 is more aggressive	[38,39]
Chromophobe RCC	5%–10%	Multiple chromosome losses	Best prognosis	[38,39]

Table 7: Regional variations (2020 data).

Region	Incidence rate (/100k)	Male:female ratio	Notable features	References
Global	4.6	2:1	6.1 (M), 3.2 (F)	[71,73]
North America	10.9	2:1	Highest incidence region	[9,45]
Europe	18.4	2.1:1	25.9 (M), 12.5 (F)	[75]
United States	16.9	2:1	81,610 new cases (2024 est.)	[53,74]

Table 8 Temporal trends and projections.

Period	Change	Key drivers	Notable exceptions	References
1975–2020	Doubled	Imaging advances (CT/MRI)	-	[9,47]
1990–2013	+23.04%	+31.2% (M), +8.8% (F)	Developing countries lag	[72]
2010–2023 (Saudi Arabia)	+176%	Improved diagnostics	Extreme regional variation	[69]
2018–2030 (projected)	−0.97% APC	Declines in developed nations	Increases in 90 countries	[43]

Table 9: Demographic patterns.

Age group	Incidence pattern	Clinical notes	References
<46 years	10% of cases	Check for hereditary syndromes	[37,58]
64 years (median)	Peak incidence	The most common diagnosis age	[49,50]
≥85 years	Increasing	Worse prognosis, advanced stages	[75]

Table 10: Risk factors.

Category	Factors	Population impact	References
Non-modifiable	Gender, male (2:1); genetic syndromes (3%–5%)	Accounts for gender disparity	[8,37]
Modifiable	Smoking (RR, 1.5), obesity (RR, 1.3), hypertension, and occupational exposures	20%–30% attributable risk	[8,45]

Table 11: Country-specific data.

Country	Notable findings	Period	References
Uruguay	Highest ASR (16.15/100k in 2017)	2017	[43]
USA	81,800 new cases (2023)	2023–2024	[53,54]
Saudi Arabia	+176% increase	2010–2023	[69]
Czech Republic	Among the highest rates	-	[64]

Table 12: Future projections (2030).

Metric	Projection	95% HDI	Key Changes	References
New cases	475,400	423,900	Increase in 172 countries	[43]
ASR (/100k)	4.46	-	Decline in 80 countries	[43]
Age patterns	Increase in 40+ age groups.	-	Decrease in <40 groups	[43]

older adults, observations have revealed potential disparities between individuals aged 60 to 70 years and those aged 70 to 80 years, including variations in their clinicopathological features and prognosis. These findings suggest that age might have a significant role in the health outcomes of older cancer patients. [91] Factors that increase kidney cancer risk include smoking, obesity, being overweight, and hypertension. [92,93] In addition, chemical exposure, family history of kidney malignancy, [94] advanced chronic kidney disease (CKD), long-term dialysis, chronic use of pain medications, noncolored, being male, and the presence of other oncology diseases, such as lymphoma infiltrating the kidneys. Smoking increases the risk of developing kidney cancer by 2-fold compared to nonsmokers. Workplace exposure to chemicals such as arsenic, some metal degreasers, or cadmium used in mining, welding, farming, and painting is another risk factor for kidney malignancy. [95,96] There are various risk factors, and the causes of RCs are not yet clear; therefore, further studies are needed to explore the underlying mechanisms.

A significant correlation was discovered between smoking cigarettes and RRC occurrence. [97] Smokers exhibited a 1.38 relative risk for RCC in comparison to those who had never smoked throughout their lives. [98] The risk of RCC was directly proportional to the dosage and correlated with the number of cigarettes consumed daily. [98] Furthermore, it was proposed that the risk was reduced after quitting smoking for more than 10 years. [98] Obesity has been identified as

a factor in RCC's existence in 141 studies and meta-analyses. [99] The meta-analysis revealed a 1.34 increase in RCC for every 5 kg/m^2 increase in the body mass index. [99] A prospective study conducted across 8 European nations, encompassing 296,638 participants, revealed a significant correlation between high blood pressure and an elevated risk of RCC. A systolic blood pressure of ≥160 mmHg was associated with a higher RCC risk compared to <120 mmHg, while a diastolic blood pressure of ≥100 mmHg compared to < 80 mmHg was associated with a higher relative risk. [100] A large study conducted on RCC patients compared with non-RCC (controls) revealed that both dialysis-dependent and chronic renal failure patients were separately linked to a higher likelihood of developing RCC. This finding was supported by previous research. [101,102] Research has shown that RCCs that arise in end-stage renal disease (ESRD) tend to have less aggressive behavior than RCCs that manifest in the overall population. [103,104] A study demonstrated that RCCs found in ESRD patients were comparatively minor (p = 0.001) and had lower grades and stages (p = 0.001) compared to RCCs detected in the general population. [103] The research found that the occurrence of PRCC was considerably more significant in patients with ESRD before kidney transplantation (17.2%) and after transplantation (27.3%) compared to the general world citizens (p = 0.01). [103] The groups did not exhibit any notable disparities in the occurrence of CCRCC. The chemicals associated with forming RCC are petroleum products, benzene, cadmium, asbestos, vinyl chloride, acetaminophen overuse, and herbicides. [105,106]

Hereditary RCCs make up 4% of cases and are more likely to occur at an early age, affect both kidneys, and involve many tumor sites. [107] VHL disease is a genetic illness inherited in an autosomal dominant manner. This condition increases the risk of developing certain types of cancers, including central nervous system hemangioblastomas, neuroendocrine tumors in the pancreas, pheochromocytomas, and primarily CC subtype RCCs. RCC occurs in 25% to 60% of VHL disease, and the size of the tumor influences the likelihood of the cancer spreading to other parts of the body. [107,108] It was shown that 27.4% of those with RCCs larger than 3 cm developed metastases in VHL disease, but no occurrences of metastases were observed in RCC patients with tumors ≤3 cm. [109] Therefore, surgical removal is recommended for RCCs≥ 3 cm in size in VHL disease. Birt-Hogg-Dube syndrome is a genetic disorder inherited dominantly and caused by mutations in the folliculin gene. This condition increases the risk of oncocytomas, cutaneous tumors, and several types of RCC, including papillary, ccRCC, and chRCC. [107] Hereditary leiomyomatosis RCC is an autosomal dominant disease, and it is due to a fumarate dehydratase gene mutation that is inherited as an autosomal dominant trait. This syndrome is associated with increased cutaneous leiomyomas, uterine leiomyomas, and type 2 PRCC in 25% to 30% of affected individuals. [107,110] Hereditary pRCC results from a mutation in the MET proto-oncogene and is characterized by its association with multiple type 1 pRCCs. Recent findings suggest a significant association between paragangliomas, pheochromocytomas, inherited succinate dehydrogenase mutations, and severe early-onset RCC. [107,111] The risk factors and the potential causes of renal tumors are summarized in **Table 13**.

Table 13: Summary of risk factors and causes of kidney tumors.

Smoking
Gender
Age
Family history of malignancy (especially kidney tumors)
Obesity and overweight
Chronic kidney disease
Chronic dialysis
Medications (non-steroidal anti-inflammatory drugs, acetaminophen overuse)
High blood pressure
Chemicals (arsenic, petroleum products, benzene, cadmium, asbestos, vinyl chloride, and herbicides)
Workplace (planting and welding)
Ethnicity and color
Other cancers (such as lymphoma)
Living area
Congenital diseases (Von Hippel-Lindau disease, hereditary leiomyomatosis)

PRESENTATIONS, DIFFERENTIAL DIAGNOSIS, AND DIAGNOSIS OF RENAL MASS

Kidney tumor presentation varies between asymptomatic and symptomatic. [97] RCC is usually asymptomatic initially when the tumor is modest (<3 cm). The clinical features depend upon the cancer stage. [112] Around 25% of individuals exhibit no symptoms, and the solid renal mass is discovered by chance during a routine radiological examination. [112] The traditional clinical triad consists of flank discomfort, hematuria, and flank tumor, which is infrequent, occurring in just 10% of individuals. The presence of this classic triad often signifies an advanced stage of illness. Hematuria or a change in urine color (dark, rusty, or brown) is uncommon and may be persistent. [113,114] Increased urine frequency, constant tiredness, loss of appetite, unexplained weight loss, anemia, hypercalcemia, and fever are all present features of kidney malignancies. [105,115] Some patients may present with pain or a dull ache in the side or lower back that is not due to an injury, and even a sizeable palpable lump in the flank or abdomen. Anemia and lower limb edema are common. Bone pain, hemoptysis, gynecomastia, and breathlessness could be present features in some kidney cancer patients who had metastasis. [116]

The primary three differential diagnoses of malignant kidney masses are renal AMLP, oncocytoma, and lymphoma. [97] The most prevalent benign kidney tumor is AMLP. AMLP comprises dysmorphic blood vessels, smooth muscle, and mature adipose tissue. [117] AMLPs are mostly sporadic but may be linked to tuberous sclerosis (TS) (<20%) or lymphangioleiomyomatosis. [118] Nearly 80% of TS patients have AMLPs, multicentric, bilateral, larger, and symptomatic lesions. [97,118,119] AMPLs commonly occur in middle-aged females, with a female:male ratio of 4:1. [120] Approximately 5% of AMLPs had inadequate lipid content, [121] which might be detectable by cross-sectional imaging. [120]

AMLP and RCC imaging appearances may overlap; hence, no radiologic result is pathognomonic. [97] Four CT characteristics distinguish lipid-poor AMLP from RCC, including a hypodense rim due to modest marginal fat, an angular interface between the tumor and normal tissue parenchyma, an unenhanced density of >38.5 HU, and homogeneous enhancement (**Figures 1** and **2**). [124] Lipid-poor AMLP is distinguished from conventional ccRCC with high accuracy, sensitivity, and specificity using unenhanced CT. [122] T1-weighted MRI could not distinguish lipid-poor AMLP from CC RCC because they contain a micro-amount of fat. [94] On the other hand, lipid-poor pRCC and AMLP exhibit low T2 signal intensity due to the hypovascularity of PRCC and the comparatively high vascularity of AMLP. [123] Tumors sized >3 cm, with calcification and intertumoral necrosis, highly suggest RCC. [123]

The second common nonmalignant renal neoplasm is oncocytoma (3%–7%). [124] The mean patient age is 68 years, the male-to-female ratio is 2.6, and the median tumor size is 3.2 cm. [125] In 95% of cases, oncocytomas were unilateral, 5% were bilateral, 6% were multi-located, and 10% were co-present with RCC. [126] Chromophobic RCC and oncocytomas share imaging and histological features. [127,128] They originate from the collecting duct. [127,128] chRCC may include imaging characteristics suggesting oncocytoma, like a well-defined border, spoke-wheel enhancement, homogenous, segmental enhancement inversion consistency, and central stellate scar (**Figure 3**). [97,127–129] To distinguish oncocytoma from CC, a corticomedullary phase TCR < 1 had high sensitivity, specificity, and accuracy, whereas a nephrographic phase TCR > 1 had lower sensitivity but greater specificity and accuracy. Despite encouraging earlier reports, a robust clinical consensus held that imaging characteristics alone cannot distinguish oncocytoma from RCC subtypes.

Primary or secondary renal lymphoma occurs. Secondary renal lymphoma is prevalent (> 30%) and usually arises after extensive lymphoma due to hematogenous dissemination or direct invasion of retroperitoneal adenopathy. [130,131] Primary Lymphoma is uncommon, comprising <1% of extranodal lymphomas. [130] Primary renal lymphoma has five CT morphologic patterns: enlarged lobular non-enhancing kidneys, bilateral multiple renal masses, retroperitoneal infiltrations, focal single non-enhancing renal mass, and bilateral diffuse non-enhancing hypodensities. [132] Multifocal lesions are most common, followed by contiguous retroperitoneal adenopathy. [130] US shows homogeneously hypoechoic, CT shows hypodense, and T1- and T2-weighted MRI show low to moderate signal intensity renal lymphoma changes (**Figure 4A–C**). [131] Due to high cellularity, kidney lymphoma has limited diffusion and poor diffusion-weighted imaging (DWI) values. However, further research is needed to see whether DWI can distinguish it from other kidney masses. [133]

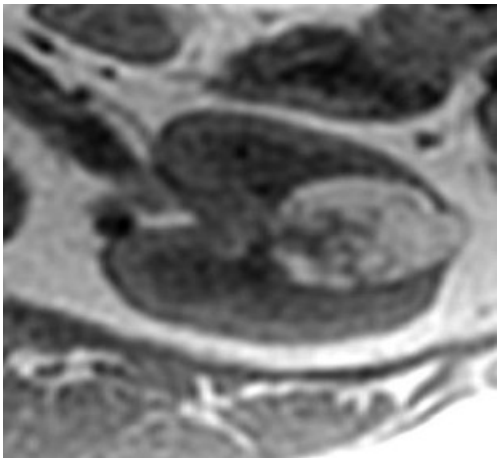

Figure 2: MRI showed a T1 hyperintense fatty lesion with moderate reticular enhancement of the non-fatty components.

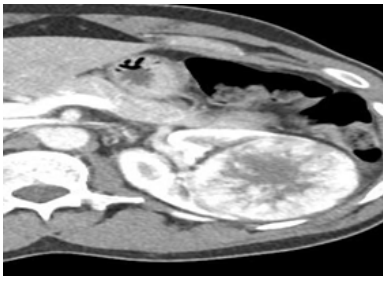

Figure 3: The left kidney shows a large central scar mass, demonstrating an oncocytoma.

Deformation of the renal shape, collecting system, ureter, and later, hydronephrosis with the displacement of adjacent tissues are rare in kidney lymphoma. [132,134] CT and MRI demonstrate hypovascularity in renal lymphoma, with lesser enhancement than the renal parenchyma. [131] Differentiating a hypovascular RCC, such as a PRCC, from a hypervascular RCC is complex, and a kidney parenchyma biopsy is often necessary. [135] Type 2 PRCC may have significant para-aortic adenopathy, mimicking secondary renal lymphoma. [136] Atypical lymphoma symptoms, including calcifications, cystic tumors, and renal vein or inferior vena cava tumor extension, suggest a different cause. [130,132,137] A renal biopsy is required if the diagnosis is unclear. Since lymphoma responds well to treatment, individuals with this condition may be able to avoid surgery.

Evaluating a renal mass requires both a detailed history and a careful physical examination. Confirming pertinent clinical symptoms, such as hematuria, flank or abdominal discomfort, and a flank mass, is highly predictive and, in most cases, diagnostic. A thorough history and examination of all potential risk factors and causes are crucial. Physical examination findings of varicocele or pedal edema may indicate vascular involvement of the tumor or invasion of the inferior vena cava. Most authors mentioned the typical RCC clinical triad (flank discomfort, hematuria, and flank [lumbar] mass), which is only reported in 6% to 10% and portends more aggressive histology and advanced disease. [105,138] On the contrary, the lumbar mass was consistently documented in all the research analyzed in the sub-Saharan area. [139–141]

Blood analysis is needed to assess the complete blood count, renal function, liver function parameters, alkaline phosphatase, and calcium. A high creatinine level warrants a renal scintigraphy to evaluate renal function. [138] Further new markers are added every day. [138,142] A CT scan is the preferred imaging method, with an accuracy of around

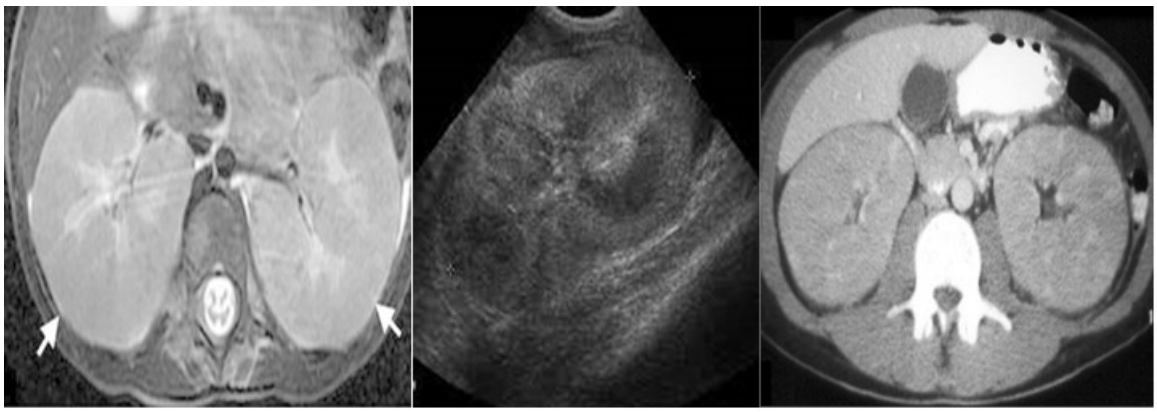

Figure 4: (A) axial MRI image shows enlarged both kidneys with multifocal cortical lesions, (B) Ultrasound shows an enlarged right kidney with cortical homogenous hypoechoic lesions. (C) Axial CT scan shows an enlarged, edematous kidney with cortical enhanced low-density lesions.

90% for detecting renal masses. A renal malignancy is highly possible when a renal tumor shows a contrast attenuation of 10 to 20 Hounsfield Units. [138] A CT scan is necessary for determining the stage of kidney carcinoma, evaluating lymph node involvement, and detecting metastases. A chest CT scan is recommended for evaluating metastases when the chest X-ray is inconclusive. MRI and Doppler ultrasonography help assess the involvement of the inferior vena cava. Studies have shown that CT scans and ultrasonography effectively diagnose and stage kidney cancers.

Different studies from the sub-Saharan area have revealed the restricted usage of intravenous urography. However, intravenous urography may be beneficial for large tumors that deform the renal parenchyma. Cystic renal lesions seen on CT scans or MRIs are classified as Bosniak class I or class II, which carry a minimal risk of malignancy and do not require further monitoring. Bosniak class IIF has a 10% chance of cancer. Hence, an ultrasound or CT follow-up is advisable. Bosniak class III has a 65% probability of malignancy, whereas Bosniak class IV has a 92% risk, and both need therapy.

Kidney tumor biomarkers

Imaging is the primary tool used for diagnosing, screening, monitoring, and assessing the effectiveness of therapy for renal tumors. Nevertheless, multiple biomarkers are available to aid in diagnosis and outcome assessment. The serum biomarkers are tumor necrosis factor receptor-associated factor-1, heat shock protein 27 (HSP27), serum amyloid A, pyruvate kinase type M2, thymidine kinase-1, and osteopontin. The urine markers are neutrophil gelatinase-associated lipocalin, nuclear matrix protein-22, aquaporin-1, kidney injury molecule-1, and perilipin 2. [105] Moreover, studying specific genes, such as the MN/CA9 gene expression of the biopsied tissue, might help in RCC diagnosis. [143] And other new markers are coming. [142] Although initial findings are promising, no serum or urine biomarker has been confirmed to diagnose renal tumors.

Imaging techniques benefit in kidney tumor diagnosis

If kidney cancer is detected, various body scans are used to determine if the cancer has spread or remains localized, including ultrasound, chest x-ray, CT scan, MRI, renal arteriogram, and radioisotope bone scan. Renal tumors exhibit diverse morphological characteristics, ranging from small, slow-growing lesions to large, invasive masses. Careful attention to specific imaging features can differentiate between the subtypes despite the wide variety of results that may be reported. [97]

The overall physical characteristics of the tumor might provide an indicator of its specific subtype. CCRCC often displays outward development and variation in its composition, such as intratumoral necrosis, cystic alteration, or bleeding, resulting in a heterogeneous appearance (**Figure 5A**). [144] In addition, it was reported that specific characteristics, such as significant size, necrosis inside the lesion, collateral blood vessels in the retroperitoneum, and thrombosis in the renal vein, were indicative of a high-grade CCRCC subtype (**Figure 5B**). [145]. Additionally, high tumor grade is highly linked to tumor capsule disruption (**Figure 5C**). [146] Approximately 70% of PRCCs are localized and found within the kidney capsule at diagnosis. These tumors are often very tiny (≤3 cm) and have a low grade. They appear as well-defined, homogeneous tumors situated at the outer edges of the kidney.

Cystic PRCCs can exhibit hemorrhagic fluid, papillary projections, and internal mural nodules. In contrast, cystic CCRCCs often have clear, non-hemorrhagic, and transparent content. Uneven walls and septations (**Figure 6A–C**). [144,145] chRCC often presents as a well-delineated and uniform tumor with little cystic change or necrosis, even in large sizes. Infiltration of the tissue surrounding the kidney and involvement of blood vessels are rare, affecting less than 4% of cases. [46,144] Additional characteristics that may differentiate between chRCC and other RCC subtypes include a spoke-wheel enhancement and a central stellate scar, although these features may also be observed in oncocytoma. [147] In certain ccRCCs, the presence of fat inside the lesion (intralesional), whether it is visible to the naked eye or only under a microscope, is a well-known characteristic. [144] Nevertheless, this discovery is not limited to a single subtype since there have been very few cases of chromophobe and pRCC-containing fat. [46,144] It was noted that all three subtypes may have microscopic fat, which may be seen as a decrease in signal intensity on opposed-phase compared to in-phase T1-weighted MRI. [46,148]

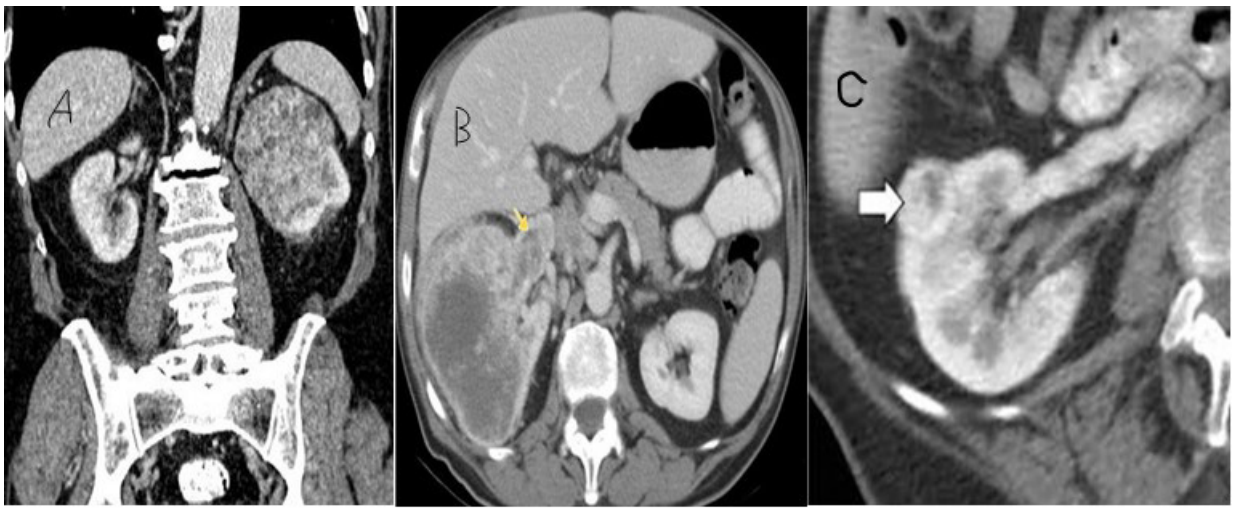

Figure 5: (A) Enhanced coronal CT scan shows a large soft tissue heterogeneous enhanced mass with cystic changes. (B) right kidney large RCC mass with vascular extension Arrowed. (C) well-defined small enhanced cortical kidney mass within the capsule.

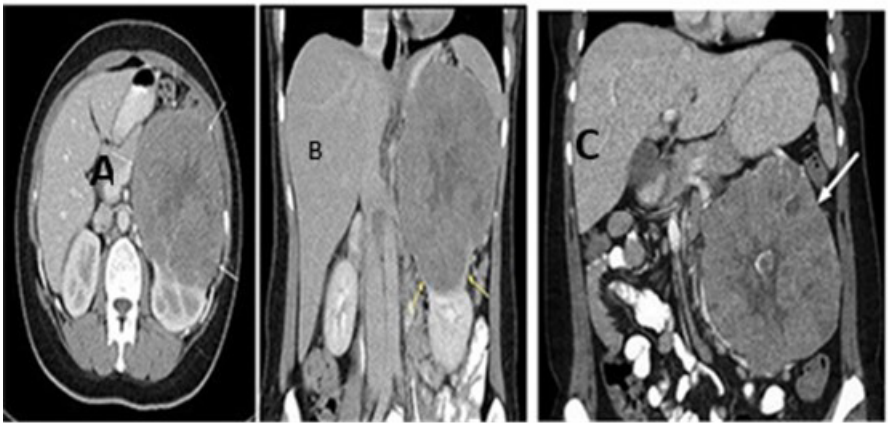

Figure 6: (A–C) Contrast-enhanced CT axial and coronal scans show a well-defined, large left renal mass with heterogeneous enhancement and areas of necrosis. The C-LEFT kidney shows a large, well-circumscribed solid tumor (arrow) with a hypoattenuating central stellate scar and internal calcification.

However, a more than 25% signal loss indicates ccRCC. In a dual-echo chemical shift T1 sequence, a straightforward two-point Dixon fat-water separation approach is often advantageous for radiologists to detect minute amounts of microscopic intralesional fat. Calcifications were much more prevalent in pRCC (32%) and chRCCs (38%) compared to ccRCC (11%). [149] pRCC has a higher prevalence of bilaterality (4%) and multifocality (22.5%) compared to ccRCC (<5%). [144,150] Nevertheless, these discoveries possess limited pragmatic significance in distinguishing subtypes.

DWI is a proven tool used by different investigators to characterize RCCs in high-grade and low-grade tumors. [151–154] A study noted a significant increase in mean apparent diffusion coefficient (ADC) values for ccRCCs compared to non-ccRCCs (p = 0.005). [151] Moreover, the lower-grade tumors had higher mean ADC values than the higher-grade tumors. [151] Chromophobe and papillary subtypes had significantly inferior mean ADC values compared to ccRCCs (p < 0.01). [151] In addition, high-grade ccRCCs had considerably lower mean ADC values compared to low-grade tumors (p = 0.021). [152] Chromophobe and PRCCs had considerably decreased mean ADC values compared to CCRCCs at 3-T scan. [154] A meta-analysis of 17 studies involving 764 patients found that ADC values on DWI significantly differentiate RCC from benign renal lesions, including oncocytoma (p < 0.0001). [97]

Several studies have recommended quantitative enhancement measures for multiphasic cross-sectional imaging to distinguish RCC subtypes. [155] pRCC is a hypervascular tumor, while chRCC has intermediate vascularity, and ccRCC is a relatively hypovascular RCC subtype. It was observed that the ccRCC enhancement mean increased during the corticomedullary phase, while that of chromophobe and pRCCs increased during the nephrographic phase. [155] ccRCC exhibits a higher mean enhancement in all stages compared to pRCC, including the nephrographic, corticomedullary, and excretory phases. The ccRCC showed more remarkable enhancement in the corticomedullary and excretory phases than chRCC

(**Figure 7**). [155] Multiphasic enhancement thresholds can differentiate between the three cell lines of RCC with 85% accuracy and 94% sensitivity. [155] A study assessed the higher maximum attenuation in CT for cc- and pRCC, which was significantly greater than ccRCC on the excretory and corticomedullary phases. [28] Meanwhile, the chRCCs showed less enhancement during the nephrographic phase than the corticomedullary phase compared to the uniform 4-phase CT technique. [122]

In contrast, Young et al. observed the opposite. [155] In a study that used multiphasic for RCC, the ccRCC had higher changes in tumor signal intensity than the other two RCC tumor subtypes (where the pRCC had the lowest change). [156] The threshold of signal intensity changes of 84% on the corticomedullary phase can be used as a distinguishing tool between cc and pRCC (96% specificity and 93% sensitivity). [156] The nephrographic and corticomedullary phases showed that the tumor-to-cortex ratio was considerably lower in papillary or chromophobe than in ccRCC. [156] Contrast-enhanced US may be a preferable alternative to CT or MRI for evaluating a renal mass. [157] This reduces the risk of contrast-induced acute kidney injury (CI-AKI) or contrast-induced nephropathy (CIN). Another advantage of contrast-enhanced US is that it can differentiate between the cystic and solid localized lesions and pseudotumors from solid neoplasms, such as an increased column of Bertin. [157] The column of Bertin, also known as the renal column or Bertin's column, is an extension of the renal cortex between the renal pyramids, supporting the pyramids and containing the blood vessels (**Figure 8A**). A study in complicated cystic renal masses reported that contrast-enhanced US was better than CT and usual transcutaneous US in determining cyst wall thickness, internal septa, and solid components (**Figure 8B**). [158]

CT perfusion analyzes the tumor's microvascular structure, including blood flow, capillary permeability, volume, and mean transit time. A study observed that CCRCCs had greater mean blood flow and volume compared to PRCCs ($p < 0.001$). Additionally, CCRCCs had a mean equivalent blood volume than chRCCs ($p < 0.001$). [159] RCCs with low microvascular density and poor prognosis have reduced blood flow and volume. Furthermore, CT perfusion may be a predictive indicator, as RCC patients with greater microvascular density have better prognoses and survival. [73,74] CT perfusion may help identify patients with metastatic RCC who may benefit from personalized anti-angiogenic therapy and measure treatment response. [160]

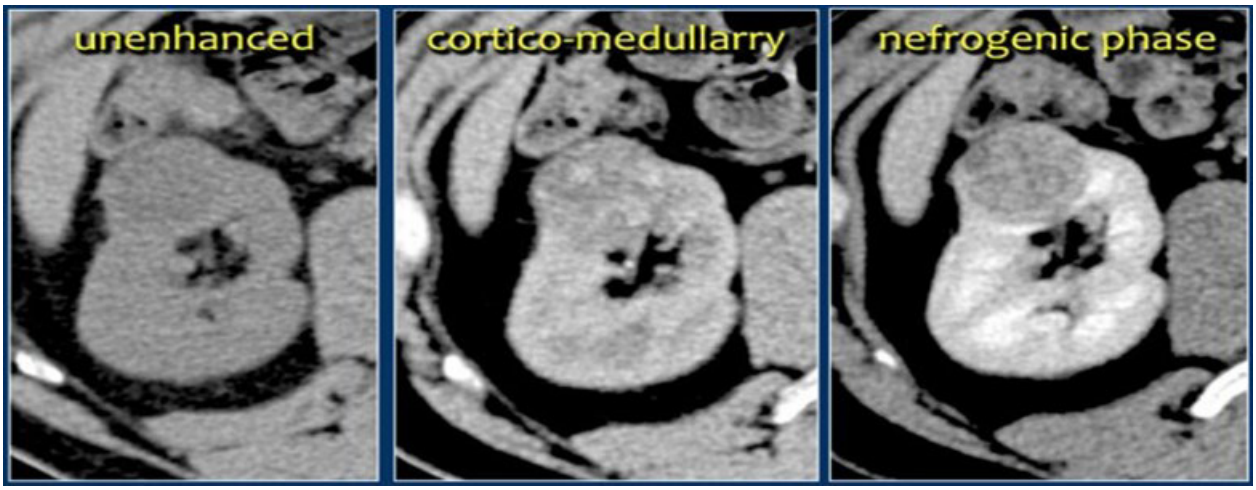

Figure 7: CT scan axial image/shows an upper kidney well-defined exophytic mass with heterogeneous enhancement (41HU pre-contrast/100HU cortico-medullary phase/80HU nephrogenic phase).

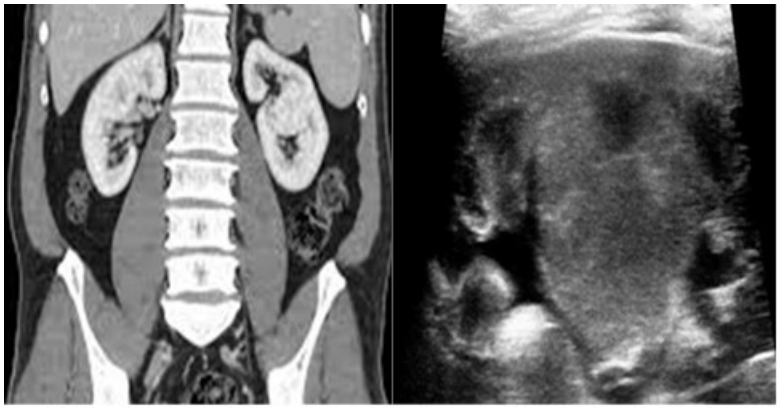

Figure 8: (A) Coronal CT scan enhanced study shows hypertrophied left kidney column of Bertin with no mass. (B) Ultrasound shows a long axial U-shaped protrusion of the renal cortex into the hilum.

Another diagnostic radiological study for RC is 18F-fluorodeoxyglucose positron emission tomography-computed tomography (FDG-PET/CT). In an early dynamic phase analysis, a study reported that ccRCCs had a higher tumor-to-normal tissue ratio and maximal standardized uptake than non-ccRCCs ($p < 0.001$). In the entire body phase, aggressive RCCs with higher stages, grades, and lymphatic or vascular invasion had higher maximal standardized uptake. [161] PET-CT is limited in initial tumor evaluation because the higher renal physiologic tracer excretion may obscure RCCs, resulting in false negatives. However, PET-CT is a valuable tool in advanced and recurrent RCC restaging. [162,163] Another study reported that PET-CT aids in determining the tumor progression rate and survival in RCC. [164] Thereby influencing clinical decision-making. Patients with positive PET-CT scans exhibit worse 5-year survival and 3-year tumor progression-free survival ($p < 0.05$) compared to those with negative PET scans in RCC patients. [163,165] A high positive uptake of a PET scan in RCC is associated with significant progression of the disease ($p < 0.05$) compared to a PET-negative scan in RCC. [163,166] Recent research has shown that in individuals with ESRD, FDG-PET/CT is beneficial for identifying RCC, and its results have revealed the potential utility of FDG-PET/CT as a screening tool for RCC. [167]

Kidney mass biopsy

Kidney mass biopsy is the most accurate method for diagnosing renal masses. [168–170] However, some reports advocated that it is possible to differentiate between nonmalignant and malignant masses and the types of malignant kidney masses radiologically. [170] The need for tissue for immunocytochemistry and cytogenetics has increased recently, as it is essential for planning therapy options and predicting prognosis. These techniques help diagnose benign and malignant neoplasms accurately, [169,170] determining RCC subtype and Fuhrman nuclear grade in some cases. [171] Others reported that a kidney mass biopsy is discretionary and should only be conducted if the histology findings might impact the treatment choice. A kidney mass biopsy is necessary to exclude metastatic malignancies in the kidney [172] or hematological malignancies, such as lymphoma, which are eligible for systemic treatment in some patients. Percutaneous ultrasonography or CT-guided core biopsy is safe. Kidney mass biopsy has good sensitivity and specificity for diagnosing RC, particularly RCC. [138] Indications of biopsy of kidney mass include extrarenal malignancy, inflammatory process causes mass, kidney mass for percutaneous stereotactic or ablation or radiotherapy, kidney mass with potential finding suggesting unresectable cancer, multiple or bilateral kidney masses, kidney mass measures <4 cm RCC, mass in a solitary kidney or transplant kidney, young patient has kidney mass (although it is controversial indication), cystic renal mass (most are nonmalignant; however, Bosniak III cystic renal mass should be biopsied. [170]

Due to the limitations of imaging tools, a kidney mass biopsy is still required for a definitive diagnosis. The Bosniak classification has enhanced the ability to distinguish between benign and possibly malignant cystic renal masses. However, it remains challenging to discriminate between malignant and nonmalignant solid kidney masses. Although efforts have been made to distinguish solid RCC from some noncancerous renal tumors, such as renal oncocytoma and fat-deficient AML, it is widely agreed that achieving this differentiation is currently not entirely feasible or replicable. [170,173] Algorithms that assess imaging results on MRI and multiphase CT have revealed a significant level of precision in diagnosing ccRCC compared to other tumors, [174,175] as well as in diagnosing pRCC compared to other tumors [176] and fat-poor AML. [177] Nevertheless, the data are obtained from a single medical facility, using a backward-looking approach and comparing cases with controls.

The use of imaging to distinguish between oncocytic masses, such as oncocytoma and chRCC, is a subject of intense debate. [127] While several researchers claim to be able to distinguish oncocytic neoplasms by imaging, others have not achieved the same success. Imaging studies for diagnosing renal masses have limitations related to their study design. These studies typically exclude uncommon histologic diagnoses and do not fully account for multiple tumors in a single patient. Furthermore, on imaging, they did not include masses in patients with hereditary kidney diseases and often overlooked pseudo lesions that resemble solid renal masses, such as anatomic variants, infection, and kidney infarction. The use of imaging to assess the grading of ccRCC, [170,178] pRCC, [179] and chRCC [180] has been examined; however, the available data are subject to the constraints above. The application of radiomics for quantitatively diagnosing kidney masses has recently gained attention and has shown promising initial results. [180] However, these findings are constrained by technical variations affecting accuracy, reproducibility, and a scarcity of high-quality multicenter trials examining outcomes. Additional study is required to determine whether imaging identification of kidney masses can completely substitute for histology diagnosis.

KIDNEY CANCER STAGING

Kidney cancer staging has different systems, including metastasis. RCC metastases most often in the lungs (60%), liver (40%), bone (40%), and brain (5%). Stage I RCC has a 5-year survival rate of 96%, stage II 82%, stage III 64%, and stage IV 23%. [97] The commonly applied systems depend on the tumor size and whether the tumor is within the kidney or has spread outside the kidney capsule. This system consists of four stages. Stage 1: The tumor is less than 7 cm in diameter and confined to the kidney. Stage 2: The tumor is > 7 cm in diameter but still confined to the kidney. Stage 3: The tumor has grown beyond the kidney into surrounding tissue and a nearby lymph node. Stage 4: The tumor has spread beyond the kidney to more than one lymph node or other body parts, such as the liver, lungs, or bones. [138] The other system depends on the primary tumor size (T), lymph node involvement (N), and the presence of distant metastasis (M). According to the American Joint Committee on Cancer Staging System, the Tumor Node Metastasis (TNM) classification was introduced. [97] This system is presented in **Table 14**.

MANAGEMENT OF RENAL TUMOR

Early discovery and treatment can save the kidney and surrounding tissues, and RCC may be curable. The tumor-spreading stage determines the chance of a cure. Even with tumors in regional lymphatics or blood arteries, many patients survived and were cured, as reported. [51,181] While distant metastases reduce disease-free lifespan, some individuals will survive following surgical removal of all tumors. About 75%

of RCC patients survive for 5 years because they are detected when the tumor is localized and surgically removable. [51] Some individuals with locally advanced or metastatic illness have had indolent histories for 3 years. [51] Sometimes, tumors recur after therapy. RCCs show spontaneous tumor regression without treatment, although it rarely happens and may not contribute to long-term survival. [51]

Avoiding risk factors such as smoking, kidney-damaging drugs, weight reduction, normalizing blood pressure, non-relative marriage, and early diagnosis of renal tumor-precipitating diseases such as VHL is crucial for reducing kidney tumor development rates. The primary treatment for kidney cancer is PNE or total nephrectomy. [182] Alone or in combination with immunotherapy, depending on the stage of the cancer at the time of presentation. However, radiation and chemotherapy are rarely used.

Stage I

The preferred surgical therapy for stage I RCC is PNE, [186] with a cure rate of 97% to 100%. [183] Current guidelines recommend elective partial nephrectomy (ePNE) as the standard surgical treatment for clinical T1a renal tumors [188] and favor ePNE over radical nephrectomy (rNE) for T1b tumors when technically feasible. [184] For larger (T2) renal tumors, radical NE is still considered the standard method; however, emerging data suggest a potential role for partial NE in select cases. [185] Localized RCC is generally treated with partial NE or nephron-sparing surgery. [138,186] Patients with cTIa renal tumors should have partial NE, as it provides favorable oncological results and reduces the likelihood of chronic kidney disease. Patients with bilateral tumors, solitary kidney tumors, or familial renal tumors should have PNE or nephron-sparing treatments. Nevertheless, ensuring a negative surgical margin should be a top focus for individuals having PNE. Advanced malignancies that cannot be treated with PNE may require rNE. For fragile elderly patients unable to tolerate surgery, thermal ablation of the kidney tumor is a viable alternative, although a biopsy is necessary before the treatment. [138] Active surveillance is recommended for certain individuals who should undergo routine imaging follow-up every 3 to 6 months. In cT1b, tumors >4 cm and <7 cm may be surgically removed with partial NE using open, laparoscopic, or robotic techniques with satisfactory oncological outcomes. If PNE is not possible, favor laparoscopic rNE over open rNE for improved postoperative pain management and recovery, and active monitoring has shown advantages in specific individuals with RCC. Ablative treatment is not recommended for this group due to the difficulty in achieving complete thermal ablation in tumors >4 cm. [138]

Patients in sub-Saharan settings may often lack PNE coverage for localized illnesses due to the limited number of urologists in the area. The scarcity of resources, high expense of active monitoring, and high rate of patients lost to follow-up make the nephron-sparing treatment less attractive in these circumstances. Radical NE may improve oncological outcomes, but may not ultimately reduce the risk of chronic kidney disease. [138]

Stage II

Either open or laparoscopic radical NE can surgically remove renal tumors >7 cm confined to the kidney. Performing an extended partial NE is not recommended in this group. [138]

Stage III

The inferior vena cava is involved in 4% to 10% of RCC. Tumors >7 cm that have not involved Gerota's fascia but affect the inferior vena cava are treated with radical NE and thrombectomy in the absence of metastasis with an acceptable mortality rate. In the case of an upper pole tumor with involvement of the adrenal gland, it is highly recommended to do NE and adrenalectomy in the same setting, since 1.9% to 7.5 % of kidney cancers involve the adrenal gland on the same side. Performing routine regional lymphadenectomy is not advised for localized illness; however, patients with N1 M0 disease should have a regional lymph node dissection. The efficacy of neoadjuvant and adjuvant treatments for RCC remains uncertain. In contrast, patients from sub-Saharan Africa often exhibit locally progressed metastatic illness, and most of them are treated with surgery because of low income. Open radical NE is often used for locally advanced RCCs in Africa. Published research in the area indicates that, on average, 74.4% of patients with renal masses had rNE.

Table 14: Renal cell carcinoma (RCC) staging based on the TNM classification system.

Stage	Tumor (T)	Lymph nodes (N)	Metastasis (M)	Description
Stage I	T1 (≤7 cm, confined to the kidney)	N0 (No lymph node involvement)	M0 (No distant metastasis)	Localized tumor within the kidney
Stage II	T2 (>7 cm, confined to the kidney)	N0	M0	Larger localized tumor
Stage III	T3 (Tumor extends into the renal vein, inferior vena cava, or perinephric tissues but not beyond Gerota's fascia)	N0	M0	Locally advanced tumor without nodal spread
Stage III	Any T	N1 (Tumor has spread to regional lymph nodes)	M0	Lymph node involvement but no distant metastasis
Stage IV	T4 (Tumor extends beyond Gerota's fascia, including the adrenal gland)	Any N	M0	Locally advanced tumor with possible lymph node spread
Stage IV	Any T	Any N	M1 (Distant metastasis present)	Cancer has spread to distantorgans (lungs, bones, liver, brain)

Tengue et al. conducted a 16-year retrospective analysis in Togo and found that 6.9% of patients needed lymph node dissection. [187]

Stage IV

The most effective way to treat tumors reaching stage IV is by undergoing surgery at specialized medical facilities, where the affected adrenal gland and parts of the liver, pancreas, or diaphragm may need to be removed if necessary. Many of these individuals already have hidden lymph node involvement that requires regional lymph node dissection. Although these actions are made, the 5-year survival rate is low, and the surgical complications of extensive removal should be considered in comparison to the cancer-fighting advantages. African studies done in Nigeria demonstrated a grim outlook for T4 illness, with an overall 1-year disease survival rate of fewer than 10% despite intervention. [140,188] The National Comprehensive Cancer Network (NCCN) reported that for stage 4 RCC patients, NE with metastasectomy, and systemic chemotherapy are rarely applicable. [189] RCCs that can be resected with many metastatic locations should receive cytoreductive NE before systemic treatment, while RCCs that cannot be surgically removed need systemic treatment. [97]

For patients with distant metastatic kidney tumors, it is advisable to undergo a cytoreductive NE. Research has shown improved outcomes when NE is paired with systemic treatment in comparison to systemic therapy alone. [190] Cytoreductive NE and interferon-alpha therapy enhance survival rates in individuals with RCC. Metastasectomy with neoadjuvant therapy has shown favorable outcomes in carefully selected individuals. [191] Metastasis to the pancreas, lungs, bone, and adrenal gland has a better prognosis. [192] Radiotherapy administered to a metastatic region, such as the brain or bone, in individuals with RCC may alleviate discomfort. [138] Chemotherapy has a restricted function as a systemic treatment in RCC, particularly in cases of metastatic CCRCC. [138] Nevertheless, gemcitabine, 5-fluorouracil, and doxorubicin have been shown to have some impact. [184]

IMMUNOTHERAPY

Immunotherapy has become a fundamental component in treating renal tumors, particularly RCC. The primary immunotherapeutic strategies include immune checkpoint inhibitors (ICIs), cytotoxic T-lymphocyte-associated protein 4 (CTLA-4) inhibitors, Cytokine Therapy, and combined therapy. [193–195]

ICIs, such as nivolumab (anti-PD-1), pembrolizumab (anti-PD-1), and avelumab (anti-PD-L1), have demonstrated efficacy in RCC by enhancing the immune system's ability to recognize and attack tumor cells.[194–196] Programmed Cell Death Protein 1 (PD-1) plays a crucial role in regulating immunological responses and promoting self-tolerance by modulating T-cell activity, inducing apoptosis in antigen-specific T cells, and inhibiting apoptosis in regulatory T cells. [197]

CTLA-4 Inhibitors (Ipilimumab), which target CTLA-4, are often combined with PD-1 inhibitors to improve therapeutic outcomes in advanced RCC. CTLA-4, also known as CD152 (cluster of differentiation 152), is a protein receptor that functions as an immune checkpoint and downregulates immune responses. [198,199]

Cytokine therapy, such as high-dose interleukin-2 (IL-2), has been utilized in select patients with metastatic RCC. However, its use is limited due to significant toxicity and the advent of more targeted therapies. [200] Combining ICIs with targeted therapies, such as tyrosine kinase inhibitors (TKIs; e.g., axitinib), has shown improved efficacy compared to monotherapies. [195,198,201]

Recent advancements also include the development of personalized cancer vaccines designed to prevent the recurrence of advanced kidney cancer. These vaccines are tailored to the genetic profile of an individual's tumor, training the immune system to recognize and eliminate residual cancer cells. Early trials have shown promising results, with patients remaining cancer-free for extended periods.

Compared to interferon-alpha alone, bevacizumab improves metastatic RCC response, regression, and survival. [184] Compared to ipilimumab, sunitinib, and nivolumab improve survival rates in treated CCRCC. [184] These medications have serious adverse effects and should be given by a multidisciplinary team. There is limited data published on systemic treatment following cytoreductive nephrectomy (CRN) for advanced or metastatic RCC in Africa. Togo [187] and Nigeria [140,141] Investigations have reported the use of immunotherapy in patients with advanced illnesses. Interferon alpha, bevacizumab, sorafenib, and sunitinib were immunotherapeutic alternatives for these studies. A study found that adjuvant immunotherapy or vascular endothelial growth factor-tyrosine kinase inhibitor (VEGF-TKIs) improved RCC prognoses. [140] All these novel therapies are expensive and have undergone extensive study. Hence, further studies are required to investigate their effectiveness and safety and discover new, more effective, and less expensive agents.

OTHER THERAPEUTIC APPROACHES

Due to tumor characteristics or patient status, certain RCs may not be surgically removed. Patients should discuss their diagnosis and associated risk factors with their healthcare provider to establish therapeutic appropriateness and safety. Alternative methods include radiofrequency ablation by Interventional radiologists or urologists. Radiofrequency ablation was formerly reserved for surgically unsuitable patients. Cryoablation, also known as cryotherapy or cryosurgery, involves freezing cancer cells.

CRN has long been a standard approach in managing metastatic RCC (mRCC). [202] However, its role has become increasingly controversial with the advent of targeted therapies and immunotherapies. [203] Combining CN with immunotherapy has historically shown a survival benefit for patients with mRCC. Two randomized controlled trials in the cytokine era supported this approach. [204] However, the introduction of targeted therapies, such as TKIs, has led to questions about the continued relevance of CN. [205] The CARMENA trial (Cancer du Rein Métastatique Nephrectomie et Antiangiogéniques [Metastatic Kidney Cancer: Nephrectomy and Anti-angiogenic Agents]), a Phase III randomized study, compared sunitinib alone with sunitinib plus CN in patients with intermediate- and high-risk medullary RCC. The results indicated that sunitinib alone was not inferior to the combination, suggesting that immediate CN may not be necessary for all patients. [206] The trial has issues,

including slow accrual, underpowering, and patient selection biases, raising concerns about the results. [206] Similarly, the SURTIME trial (Surgery after Sunitinib Malate in Treating Patients with Metastatic Kidney Cancer) evaluated immediate versus deferred CN in patients receiving sunitinib. Although limited by low accrual, the study suggested that deferred CN after initial systemic therapy might offer better overall survival compared to immediate surgery. [207]

These findings have led to a paradigm shift, emphasizing the importance of patient selection. Factors such as performance status, tumor burden, and metastatic distribution are critical in determining the appropriateness of CN. [203] Current guidelines suggest that while CN remains a viable option, it should be considered on a case-by-case basis, particularly in patients with favorable prognostic features. [202] As systemic therapies continue to evolve, ongoing research is needed to clarify the role of CN in the era of immunotherapies and targeted treatments. [204] Future trials should focus on identifying biomarkers and clinical characteristics that predict which patients will benefit from surgical intervention. [205] Some surgeons utilize this method with laparoscopy to treat tumors, although long-term evidence is limited.

FOLLOW-UP

Post-surgical follow-up should be based on individual risk assessment. Low-risk patients should undergo imaging (CT, MRI, or ultrasound) within one year following surgery. Chest X-rays should be performed yearly for the first 3–6 years to check for metastasis. Moderate-to-high-risk patients will require an MRI or CT scan 6 months after surgery. A yearly chest X-ray or chest CT scan is advisable for up to 5 years. [138] However, the NCCN recommends baseline chest, abdomen, and pelvic CT or MRI pre-treatment or pre-observation for stage IV patients, followed by repeat imaging every 6 to 16 weeks per physician judgment and patient clinical status. [189] Based on disease change and active locations, imaging frequency may be adjusted. [97,208]

OUTCOME

It was reported that CT perfusion may be a predictive indicator, as RCC patients with greater microvascular density had better prognoses and survival. [73,74] CT perfusion may help identify patients with metastatic RCC who may benefit from personalized anti-angiogenic therapy and measure treatment response. Based on preoperative imaging, a systematic review determined the optimal therapy for localized kidney tumors at higher clinical stages (T1b and T2). It noted that removing just the tumor and keeping the kidney may be an effective cancer therapy that preserves renal function. However, kidney-sparing surgery for large tumors increases the perioperative complication rate. [209]

After NE, the incidence of RCC recurrence has been reported to be 7%, with a median time to recurrence of 38 months for T1 tumors, 26% with a median time to recurrence of 32 months for T2 disease, and 39% with a median time to recurrence of 17 months for T3 tumors. [210] The reported data revealed that there is a heterogeneous perioperative mortality after radical NE in sub-Saharan Africa. However, studies in Nigeria, [188] Mali, [139] and Togo [211] reported 5.1% perioperative mortality after radical NE. These fatalities were mostly from perioperative bleeding or pulmonary complications. These figures are similar to a Nigerian comprehensive analysis of RCC that found 6.3% to 7.8% perioperative mortality following rNE. [212] These values exceed the 2.8% perioperative mortality of radical nephrectomies in Europe and North America. [212] This poor outcome was due to late presentation, a lack of nephron-sparing competence, and an under-equipped critical care unit. Uro-oncological care in these areas requires substantial funding, advanced imaging and diagnostics, and skilled personnel to foster a multidisciplinary approach. Urologists, radiation oncologists, medical oncologists, and radiologists should collaborate to provide the best treatment and follow realistic, viable, and evidence-based guidelines. According to Cassell et al., only accurate documentation and organized African research committees and groups can initiate this. [138]

Extrapolating RCC's 5-year overall survival after therapy is difficult because of heterogeneous reporting. A retrospective Kaplan–Meier analysis showed 46% 5-year survival for young and 26% for older RCC patients, [213] whereas another found the 5-year RCC survival to be <10% after rNE. [140] Awareness campaigns, practical cancer therapy guidelines, and subregion cancer registries are needed to attain 55% and 73% 5-year overall survival rates, as in Europe and the US, respectively. [212] Quality of life is usually affected in cancer patients due to chemotherapy, tumor complications, and other associated comorbidities. Radial or partial kidney excision affects the quality of life during perioperative and in the long term by causing chronic kidney disease and chronic renal failure, affecting patients' survival rates. [214]

CONCLUSIONS

A multidisciplinary approach facilitates the diagnosis, staging, and treatment. Differentiation between the types of kidney masses is usually essential and may require histological examination; however, it is not commonly required. Radiological investigations, including ultrasound, computed tomography, MRI, and positron emission tomography scans, are helpful for the detection, diagnosis, and prediction of outcomes. Early detection and resection are often curative in more than 97% of cases. Different risk factors and causes for kidney tumors should be explored and avoided. Nephrons-reserving PNE with a safe margin is preferable, resulting in fewer complications; however, the therapeutic approach is usually guided by the tumor stage at presentation. Guidelines propose active monitoring, thermal ablation, PNE, rNE, cytoreductive surgery, and immunotherapy at distinct stages of RCC. Due to the therapy's applicability at various stages, decreased follow-up costs, and cost-effectiveness, open radical nephrectomy is most widely used in low-income communities. Better outcomes are usually achievable in developed communities; however, the prognosis is dismal despite surgery in low-income nations since most patients have advanced tumors at presentation, and the other non-surgical therapeutic options are not widely available.

AUTHORS' CONTRIBUTION

All authors have significantly contributed to the work, whether by conducting literature searches, drafting, revising, or critically reviewing the article. They have given their final approval of the version to be published, have agreed with the

journal to which the article has been submitted, and agree to be accountable for all aspects of the work.

SOURCE OF FUNDING

The authors acknowledge the support of the Libyan Open University.

CONFLICT OF INTEREST

None.

REFERENCES

1. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2018. CA Cancer J Clin. 2018;68:7-30.
2. Inamura K. Renal cell tumors: Understanding their molecular pathological epidemiology and the 2016 WHO classification. Int J Mol Sci. 2017;18(10):2195.
3. Humphrey PA, Moch H, Cubilla AL, Ulbright TM, Reuter VE. The 2016 WHO classification of tumours of the urinary system and male genital organs-Part B: Prostate and bladder tumours. Eur Urol. 2016;70(1):106-119.
4. Garfield K, LaGrange CA. Renal cell cancer. [Updated 2023 Jul 31]. In: StatPearls [Internet]. Treasure Island, FL: StatPearls Publishing; 2024. Available from: https://www.ncbi.nlm.nih.gov/books/NBK470336/
5. Cancer Council Australia. Types of kidney cancer [Internet]. Cancer Council Australia; [cited 2024 Apr]. Available from: https://www.cancer.org.au/cancer-information/types-of-cancer/kidney-cancer
6. Robertson S. Renal cell cancer survival rate [Internet]. 2023 [cited 2024 Apr]. Available from: https://www.news-medical.net/health/Renal-Cell-Carcinoma-Survival-Rate.aspx
7. Pandey J, Syed W. Renal cancer. [Updated 2024 Oct 4]. In: StatPearls [Internet]. Treasure Island, FL: StatPearls Publishing; 2025.
8. Padala SA, Barsouk A, Thandra KC, Saginala K, Mohammed A, Vakiti A, et al. Epidemiology of renal cell carcinoma. World J Oncol. 2020;11(3):79-87.
9. Moch H, Amin MB, Berney DM, Compérat EM, Gill AJ, Hartmann A, et al. The 2022 World Health Organization Classification of Tumours of the Urinary System and Male Genital Organs-Part A: Renal, penile, and testicular tumours. Eur Urol. 2022;82(5):458-468.
10. Piazza P, Bianchi L, Fiorentino M, Gaudiano C, Giunchi F, Brunocilla E, et al. The new classification of renal cell carcinoma: What is the clinical issue? Minerva Urol Nephrol. 2023;75(3):269-271.
11. Eble JN, Sauter G, Epstein JI, Sesterhenn IA, eds. Pathology and Genetics of Tumours of the Urinary System and Male Genital Organs. Lyon: IARC Press; 2004.
12. Clark DJ, Dhanasekaran SM, Petralia F, Pan J, Song X, Hu Y, et al. Integrated proteogenomic characterization of clear cell renal cell carcinoma. Cell. 2019;179(4):964-983.e31.
13. Turajlic S, Xu H, Litchfield K, Rowan A, Chambers T, Lopez JI, et al. Tracking cancer evolution reveals constrained routes to metastases: TRACERx renal. Cell. 2018;173(3):581-594.e12.
14. International Agency for Research on Cancer. WHO Classification of Tumours of the Urinary System and Male Genital Organs. 5th ed. Lyon: IARC; 2022.
15. Argani P, Reuter VE, Zhang L, Sung YS, Ning Y, Epstein JI, et al. TFEB-amplified renal cell carcinomas: An aggressive molecular subset demonstrating variable melanocytic marker expression and morphologic heterogeneity. Am J Surg Pathol. 2016;40(11):1484-1495.
16. Sukov WR, Hodge JC, Lohse CM, Akre MK, Leibovich BC, Thompson RH, et al. ALK alterations in adult renal cell carcinoma: Frequency, clinicopathologic features and outcome in a large series of consecutively treated patients. Mod Pathol. 2012;25(11):1516-1525.
17. Shah RB, Stohr BA, Tu ZJ, Gao Y, Przybycin CG, Nguyen J, et al. "Renal cell carcinoma with leiomyomatous stroma" harbor somatic mutations of TSC1, TSC2, MTOR, and/or ELOC (TCEB1): Clinicopathologic and molecular characterization of 18 sporadic tumors supports a distinct entity. Am J Surg Pathol. 2020;44(5):571-581.
18. Wang B, Martini-Stoica H, Qi C, Lu TC, Wang S, Xiong W, et al. TFEB-vacuolar ATPase signaling regulates lysosomal function and microglial activation in tauopathy. Nat Neurosci. 2024;27(1):48-62.
19. Choueiri TK, Cheville J, Palescandolo E, Fay AP, Kantoff PW, Atkins MB, et al. BRAF mutations in metanephric adenoma of the kidney. Eur Urol. 2012;62(5):917-922.
20. Batavia AA, Schraml P, Moch H. Clear cell renal cell carcinoma with wild-type von Hippel-Lindau gene: A non-existent or new tumour entity? Histopathology. 2019;74(1):60-67.
21. Irmisch A, Bonilla X, Chevrier S, Lehmann KV, Singer F, Toussaint NC, et al. The Tumor Profiler Study: Integrated, multi-omic, functional tumor profiling for clinical decision support. Cancer Cell. 2021;39(3):288-293.
22. Palsgrove DN, Li Y, Pratilas CA, Lin MT, Pallavajjalla A, Gocke C, et al. Eosinophilic solid and cystic (ESC) renal cell carcinomas harbor TSC mutations: Molecular analysis supports an expanding clinicopathologic spectrum. Am J Surg Pathol. 2018;42(9):1166-1181.
23. Yunker A, Holder L, Nething J. Newly described eosinophilic, solid and cystic renal cell carcinoma: A case report and review of the literature. Arch Nephrol Urol. 2020;3:038-045.
24. Hakimi AA, Tickoo SK, Jacobsen A, Sarungbam J, Sfakianos JP, Sato Y, et al. TCEB1-mutated renal cell carcinoma: A distinct genomic and morphological subtype. Mod Pathol. 2015;28(6):845-853.
25. Tao JJ, Wei G, Patel R, Fagan P, Hao X, Bridge JA, et al. ALK fusions in renal cell carcinoma: Response to entrectinib. JCO Precis Oncol. 2018;2:1-8.
26. Jia L, Carlo MI, Khan H, Nanjangud GJ, Rana S, Cimera R, et al. Distinctive mechanisms underlie the loss of SMARCB1 protein expression in renal medullary carcinoma: Morphologic and molecular analysis of 20 cases. Mod Pathol. 2019;32(9):1329-1343.
27. Colombo P, Smith SC, Massa S, Renne SL, Brambilla S, Peschechera R, et al. Unclassified renal cell carcinoma with medullary phenotype versus renal medullary carcinoma: Lessons from diagnosis in an Italian man found to harbor sickle cell trait. Urol Case Rep. 2015;3(6):215-218.
28. Msaouel P, Slack-Tidwell R, Genovese G, Daw N, Siefker-Radtke A, Tannir NM. Phase II trial of ixazomib combined with gemcitabine and doxorubicin in patients with SMARCB1-deficient kidney malignancies. J Clin Oncol. 2019;37(7):TPS678-TPS678.

29. Yu L, Li J, Xu S, Navia Miranda M, Wang G, Duan Y. An Xp11.2 translocation renal cell carcinoma with SMARCB1 (INI1) inactivation in adult end-stage renal disease: A case report. Diagn Pathol. 2016;11(1):98.
30. Moch H, Cubilla AL, Humphrey PA, Reuter VE, Ulbright TM. The 2016 WHO classification of tumours of the urinary system and male genital organs-part A: Renal, penile, and testicular tumours. Eur Urol. 2016;70(1):93-105.
31. Smith SC, Sirohi D, Ohe C, McHugh JB, Hornick JL, Kalariya J, et al. A distinctive, low-grade oncocytic fumarate hydratase-deficient renal cell carcinoma, morphologically reminiscent of succinate dehydrogenase-deficient renal cell carcinoma. Histopathology. 2017;71(1):42-52.
32. Trpkov K, Hes O, Agaimy A, Bonert M, Martinek P, Magi-Galluzzi C, et al. Fumarate hydratase-deficient renal cell carcinoma is strongly correlated with fumarate hydratase mutation and hereditary leiomyomatosis and renal cell carcinoma syndrome. Am J Surg Pathol. 2016;40(7):865-875.
33. Wyvekens N, Valtcheva N, Mischo A, Helmchen B, Hermanns T, Choschzick M, et al. Novel morphological and genetic features of fumarate hydratase deficient renal cell carcinoma in HLRCC syndrome patients with a tailored therapeutic approach. Genes Chromosomes Cancer. 2020;59(11):611-619.
34. Srinivasan R, Su D, Stamatakis L, Siddiqui MM, Singer E, Shuch B, et al. 5 Mechanism based targeted therapy for hereditary leiomyomatosis and renal cell cancer (HLRCC) and sporadic papillary renal cell carcinoma: Interim results from a phase 2 study of bevacizumab and erlotinib. Eur J Cancer. 2014;50(6).
35. Hsieh JJ, Purdue MP, Signoretti S, Swanton C, Albiges L, Schmidinger M, et al. Renal cell carcinoma. Nat Rev Dis Primers. 2017;3:17009.
36. Choueiri TK, Motzer RJ. Systemic therapy for metastatic renal-cell carcinoma. N Engl J Med. 2017;376(4): 354-366.
37. Patard JJ, Leray E, Rioux-Leclercq N, Cindolo L, Ficarra V, Zisman A, et al. Prognostic value of histologic subtypes in renal cell carcinoma: A multicenter experience. J Clin Oncol. 2005;23(12):2763-2771.
38. Abu-Ghanem Y, Powles T, Capitanio U, Beisland C, Järvinen P, Stewart GD, et al. The impact of histological subtype on the incidence, timing, and patterns of recurrence in patients with renal cell carcinoma after surgery-Results from RECUR Consortium. Eur Urol Oncol. 2021;4(3):473-482.
39. Alkhateeb SS, Alothman AS, Addar AM, Alqahtani RA, Mansi TM, Masuadi EM. Kidney cancer in Saudi Arabia. A 25-year analysis of epidemiology and risk factors in a tertiary center. Saudi Med J. 2018;39(5):459-463.
40. Ikuemonisan J, Togun A, Oyejinmi I, Bakare A, Adejoro O. Influence of histologic types and subtypes on survival outcomes of intermediate-high and high-risk renal cell carcinoma following nephrectomy: Findings from the SEER Database. Urology. 2022;159:146-151.
41. Du Z, Chen W, Xia Q, Shi O, Chen Q. Trends and projections of kidney cancer incidence at the global and national levels, 1990-2030: A Bayesian age-period-cohort modeling study. Biomark Res. 2020;8:16.
42. Wong MCS, Goggins WB, Yip BHK, Fung FDH, Leung C, Fang Y, et al. Incidence and mortality of kidney cancer: Temporal patterns and global trends in 39 countries. Sci Rep. 2017;7(1):15698.
43. Makino T, Kadomoto S, Izumi K, Mizokami A. Epidemiology and prevention of renal cell carcinoma. Cancers (Basel). 2022;14(16):4059.
44. Bukavina L, Bensalah K, Bray F, Carlo M, Challacombe B, Karam JA, et al. Epidemiology of Renal Cell Carcinoma: 2022 Update. Eur Urol. 2022;82(5):529-542.
45. Ridge CA, Pua BB, Madoff DC. Epidemiology and staging of renal cell carcinoma. Semin Intervent Radiol. 2014;31(1):3-8.
46. Muglia VF, Prando A. Renal cell carcinoma: Histological classification and correlation with imaging findings. Radiol Bras. 2015;48(3):166-174.
47. Mahasin SZ, Aloudah N, Al-Surimi K, Alkhateeb SS. Epidemiology profile of renal cell carcinoma: A 10-year patients' experience at King Abdulaziz Medical City, National Guard Health Affairs, Saudi Arabia. Urol Ann. 2018;10(1):59-64.
48. Thorstenson A, Bergman M, Scherman-Plogell AH, Hosseinnia S, Ljungberg B, Adolfsson J, et al. Tumour characteristics and surgical treatment of renal cell carcinoma in Sweden 2005–2010: A population-based study from the National Swedish Kidney Cancer Register. Scand J Urol. 2014;48(3):231-238.
49. Torre LA, Bray F, Siegel RL, Ferlay J, Lortet-Tieulent J, Jemal A. Global cancer statistics, 2012. CA Cancer J Clin. 2015;65:87-108.
50. Global Burden of Disease Cancer Collaboration; Fitzmaurice C, Dicker D, Pain A, Hamavid H, Moradi-Lakeh M, et al. The Global Burden of Cancer 2013. JAMA Oncol. 2015;1:505-527.
51. National Cancer Institute. Kidney and Renal Pelvis Cancer. Bethesda, MD: National Cancer Institute; [cited 2024 Apr]. Available from: https://seer.cancer.gov/statfacts/html/kidrp.html
52. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2016. CA Cancer J Clin. 2016;66:7-30.
53. Ferlay J, Steliarova-Foucher E, Lortet-Tieulent J, Rosso S, Coebergh JW, Comber H, et al. Cancer incidence and mortality patterns in Europe: Estimates for 40 countries in 2012. Eur J Cancer. 2013;49:1374-1403.
54. Aziz A, May M, Zigeuner R, Pichler M, Chromecki T, Cindolo L, et al. Do young patients with renal cell carcinoma feature a distinct outcome after surgery? A comparative analysis of patient age based on the multinational CORONA database. J Urol. 2014;191(2):310-315.
55. King SC, Pollack LA, Li J, King JB, Master VA. Continued increase in incidence of renal cell carcinoma, especially in young patients and high grade disease: United States 2001 to 2010. J Urol. 2014;191(6):1665-1670.
56. Palumbo C, Pecoraro A, Rosiello G, Luzzago S, Deuker M, Stolzenbach F, et al. Renal cell carcinoma incidence rates and trends in young adults aged 20-39 years. Cancer Epidemiol. 2020;67:101762.
57. Sun M, Thuret R, Abdollah F, Lughezzani G, Schmitges J, Tian Z, et al. Age-adjusted incidence, mortality, and survival rates of stage-specific renal cell carcinoma in North America: A trend analysis. Eur Urol. 2011;59(1): 135-141.
58. Cumberbatch MG, Rota M, Catto JW, La Vecchia C. The role of tobacco smoke in bladder and kidney carcinogenesis: A comparison of exposures and meta-analysis of incidence and mortality risks. Eur Urol. 2016;70(3):458-466.

59. Maher ER. Hereditary renal cell carcinoma syndromes: Diagnosis, surveillance and management. World J Urol. 2018;36(12):1891-1898.
60. Schmidt LS, Linehan WM. Genetic predisposition to kidney cancer. Semin Oncol. 2016;43(5):566-574.
61. Mikhail MI, Singh AK. Von Hippel-Lindau Syndrome. [Updated 2023 Jan 30]. In: StatPearls [Internet]. Treasure Island, FL: StatPearls Publishing; 2025.
62. Yu Y, Zheng M, Zhu W, Zhao F, Guan B, Shen Q, et al. Hereditary leiomyomatosis and renal cell cancer (HLRCC): Case series and review of the literature. Urol Oncol. 2021;39(11):791.e9-791.e16.
63. Crane JS, Rutt V, Oakley AM. Birt-Hogg-Dube Syndrome. [Updated 2023 Jul 4]. In: StatPearls [Internet]. Treasure Island, FL: StatPearls Publishing; 2025.
64. Furuya M, Hasumi H, Yao M, Nagashima Y. Birt-Hogg-Dubé syndrome-associated renal cell carcinoma: Histopathological features and diagnostic conundrum. Cancer Sci. 2020;111(1):15-22.
65. Jacoba IM, Lu Z. Hereditary papillary renal cell carcinoma. Semin Diagn Pathol. 2024;41(1):28-31.
66. Cirillo L, Innocenti S, Becherucci F. Global epidemiology of kidney cancer. Nephrol Dial Transplant. 2024;39: 920-928.
67. Sung WW, Ko PY, Chen WJ, Wang SC, Chen SL. Trends in the kidney cancer mortality-to-incidence ratios according to health care expenditures of 56 countries. Sci Rep. 2021;11:1479.
68. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2018;68(6): 394-424.
69. Capitanio U, Bensalah K, Bex A, Boorjian SA, Bray F, Coleman J, et al. Epidemiology of renal cell carcinoma. Eur Urol. 2019;75(1):74-84.
70. Zuo S, Wang L, Wen Y, Dai G. Identification of a universal 6-lncRNA prognostic signature for three pathologic subtypes of renal cell carcinoma. J Cell Biochem. 2019;120:7375-7385.
71. Washio M, Mori M, Mikami K, Miki T, Watanabe Y, Nakao M, et al. Risk factors for renal cell carcinoma in a Japanese population. Asian Pac J Cancer Prev. 2014;15(21):9065-9070.
72. Fidler MM, Gupta S, Soerjomataram I, Ferlay J, Steliarova-Foucher E, Bray F. Cancer incidence and mortality among young adults aged 20-39 years worldwide in 2012: A population-based study. Lancet Oncol. 2017;18(12):1579-1589.
73. Abomelha MS. Trends of genitourinary cancer among Saudis. Arab J Urol. 2011;9(3):199-202.
74. Alasker A, Alnafisah TR, Alghafees M, Sabbah BN, Shafqat A, Alhaider A, et al. Exploring renal malignancies in Saudi Arabia: Insights from a tertiary care center study. J Kidney Cancer VHL. 2023;10(4):13-19.
75. Scelo G, Li P, Chanudet E, Muller DC. Variability of sex disparities in cancer incidence over 30 years: The striking case of kidney cancer. Eur Urol Focus. 2018;4:586-590.
76. Palumbo C, Pecoraro A, Knipper S, Rosiello G, Luzzago S, Deuker M, et al. Contemporary age-adjusted incidence and mortality rates of renal cell carcinoma: Analysis according to gender, race, stage, grade, and histology. Eur Urol Focus. 2021;7(3):644-652.
77. Dy GW, Gore JL, Forouzanfar MH, Naghavi M, Fitzmaurice C. Global Burden of Urologic Cancers, 1990-2013. Eur Urol. 2017;71:437-446.
78. WHO. Cancer today. [cited Mar 2025]. Available from: https://gco.iarc.fr/today/home
79. American Cancer Society. Explore cancer statistics. [cited May 2025]. Available from: https://cancerstatisticscenter.cancer.org/
80. ECIS - European Cancer Information System. Browse ECIS data and publications. [cited Apr 2025]. Available from: https://ecis.jrc.ec.europa.eu/
81. Sung H, Siegel RL, Torre LA, Pearson-Stuttard J, Islami F, Fedewa SA, et al. Global patterns in excess body weight and the associated cancer burden. CA Cancer J Clin. 2019;69(2):88-112.
82. Douglas I, Forbes H, dos-Santos-Silva I, Leon DA, Smeeth L. Body-mass index and risk of 22 specific cancers: A population-based cohort study of 5·24 million UK adults. Lancet. 2014;384(9945):755-765.
83. Lipworth L, Tarone RE, McLaughlin JK. Renal cell cancer among African Americans: An epidemiologic review. BMC Cancer. 2011;11:133.
84. Znaor A, Lortet-Tieulent J, Laversanne M, Jemal A, Bray F. International variations and trends in renal cell carcinoma incidence and mortality. Eur Urol. 2015;67(3):519-530.
85. Liu Z, Jiang Y, Fang Q, Yuan H, Cai N, Suo C, et al. Future of cancer incidence in Shanghai, China: Predicting the burden upon the ageing population. Cancer Epidemiol. 2019;60:8-15.
86. Chow WH, Dong LM, Devesa SS. Epidemiology and risk factors for kidney cancer. Nat Rev Urol. 2010;7(5): 245-257.
87. Rossi SH, Prezzi D, Kelly-Morland C, Goh V. Imaging for the diagnosis and response assessment of renal tumours. World J Urol. 2018;36(12):1927-1942.
88. Heilbrun ME, Yu J, Smith KJ, Dechet CB, Zagoria RJ, Roberts MS. The cost-effectiveness of immediate treatment, percutaneous biopsy and active surveillance for the diagnosis of the small solid renal mass: Evidence from a Markov model. J Urol. 2012;187(1):39-43.
89. O'Connor E, Timm B, Lawrentschuk N, Ischia J. Open partial nephrectomy: Current review. Transl Androl Urol. 2020;9(6):3149-3159.
90. Peng X, Sun H, Wang L, Guo W, Zhao Z, Yang J. Analysis of clinical characteristics and prognostic factors of elderly patients with renal cell carcinoma based on the SEER database. Medicine (Baltimore). 2023;102(25): e34069.
91. Wang Y, Zhang HX, Zhang H, He HY. [Clinicopathological characteristics and prognosis of young patients with upper tract urethelial carcinoma]. Zhonghua Bing Li Xue Za Zhi. 2021;50(2):90-96.
92. Hötker AM, Karlo CA, Di Paolo PL, Zheng J, Moskowitz CS, Russo P, et al. Renal cell carcinoma: Associations between tumor imaging features and epidemiological risk factors. Eur J Radiol. 2020;129:109096.
93. Tahbaz R, Schmid M, Merseburger AS. Prevention of kidney cancer incidence and recurrence: Lifestyle, medication and nutrition. Curr Opin Urol. 2018;28(1): 62-79.
94. Taneja SS. Re: Large prospective investigation of meat intake, related mutagens, and risk of renal cell carcinoma. J Urol. 2012;187(6):2022-2023.

95. Stein CJ, Colditz GA. Modifiable risk factors for cancer. Br J Cancer. 2004;90:299-303.
96. Cani M, Turco F, Butticè S, Vogl UM, Buttigliero C, Novello S, et al. How does environmental and occupational exposure contribute to carcinogenesis in genitourinary and lung cancers? Cancers (Basel). 2023;15(10):2836.
97. Low G, Huang G, Fu W, Moloo Z, Girgis S. Review of renal cell carcinoma and its common subtypes in radiology. World J Radiol. 2016;8(5):484-500.
98. Hunt JD, van der Hel OL, McMillan GP, Boffetta P, Brennan P. Renal cell carcinoma in relation to cigarette smoking: Meta-analysis of 24 studies. Int J Cancer. 2005;114(1):101-108.
99. Renehan AG, Tyson M, Egger M, Heller RF, Zwahlen M. Body-mass index and incidence of cancer: A systematic review and meta-analysis of prospective observational studies. Lancet. 2008;371(9612):569-578.
100. Weikert S, Boeing H, Pischon T, Weikert C, Olsen A, Tjonneland A, et al. Blood pressure and risk of renal cell carcinoma in the European prospective investigation into cancer and nutrition. Am J Epidemiol. 2008;167(4): 438-446.
101. Hofmann JN, Schwartz K, Chow WH, Ruterbusch JJ, Shuch BM, Karami S, et al. The association between chronic renal failure and renal cell carcinoma may differ between Black and White Americans. Cancer Causes Control. 2013;24(1):167-174.
102. Hofmann JN, Purdue MP. CKD and risk of renal cell carcinoma: A causal association? J Am Soc Nephrol. 2014;25(10):2147-2148.
103. Breda A, Lucarelli G, Rodriguez-Faba O, Guirado L, Facundo C, Bettocchi C, et al. Clinical and pathological outcomes of renal cell carcinoma (RCC) in native kidneys of patients with end-stage renal disease: A long-term comparative retrospective study with RCC diagnosed in the general population. World J Urol. 2015;33(1):1-7.
104. Neuzillet Y, Tillou X, Mathieu R, Long JA, Gigante M, Paparel P, et al. Renal cell carcinoma (RCC) in patients with end-stage renal disease exhibits many favourable clinical, pathologic, and outcome features compared with RCC in the general population. Eur Urol. 2011;60(2): 366-373.
105. Pastore AL, Palleschi G, Silvestri L, Moschese D, Ricci S, Petrozza V, et al. Serum and urine biomarkers for human renal cell carcinoma. Dis Markers. 2015;2015:251403.
106. Hu J, Mao Y, White K. Renal cell carcinoma and occupational exposure to chemicals in Canada. Occup Med (Lond). 2002;52(3):157-164.
107. Byler TK, Bratslavsky G. Hereditary renal cell carcinoma: Genetics, clinical features, and surgical considerations. World J Urol. 2014;32(3):623-630.
108. Lonser RR, Glenn GM, Walther M, Chew EY, Libutti SK, Linehan WM, et al. von Hippel-Lindau disease. Lancet. 2003;361(9374):2059-2067.
109. Duffey BG, Choyke PL, Glenn G, Grubb RL, Venzon D, Linehan WM, et al. The relationship between renal tumor size and metastases in patients with von Hippel-Lindau disease. J Urol. 2004;172(1):63-65.
110. Toro JR, Nickerson ML, Wei MH, Warren MB, Glenn GM, Turner ML, et al. Mutations in the fumarate hydratase gene cause hereditary leiomyomatosis and renal cell cancer in families in North America. Am J Hum Genet. 2003;73(1):95-106.
111. Ricketts CJ, Shuch B, Vocke CD, Metwalli AR, Bratslavsky G, Middelton L, et al. Succinate dehydrogenase kidney cancer: An aggressive example of the Warburg effect in cancer. J Urol. 2012;188(6):2063-2071.
112. Garfield K, LaGrange CA. Renal cell cancer. [Updated 2023 Jul 31]. In: StatPearls [Internet]. Treasure Island, FL: StatPearls Publishing; 2024.
113. Bukhari S, Amodu A, Akinyemi M, Wallach S. Persistent hematuria caused by renal cell carcinoma after aortic valve replacement and warfarin therapy. Proc (Bayl Univ Med Cent). 2017;30(3):327-329.
114. Davis R, Jones JS, Barocas DA, Castle EP, Lang EK, Leveillee RJ, et al. Diagnosis, evaluation and follow-up of asymptomatic microhematuria (AMH) in adults: AUA guideline. J Urol. 2012;188(6 Suppl):2473-2481.
115. Ward RD, Tanaka H, Campbell SC, Remer EM. 2017 AUA renal mass and localized renal cancer guidelines: Imaging implications. Radiographics. 2018;38(7):2021-2033.
116. Krabbe LM, Bagrodia A, Margulis V, Wood CG. Surgical management of renal cell carcinoma. Semin Intervent Radiol. 2014;31(1):27-32.
117. Jinzaki M, Silverman SG, Akita H, Nagashima Y, Mikami S, Oya M. Renal angiomyolipoma: A radiological classification and update on recent developments in diagnosis and management. Abdom Imaging. 2014;39(3):588-604.
118. Logue LG, Acker RE, Sienko AE. Best cases from the AFIP: Angiomyolipomas in tuberous sclerosis. Radiographics. 2003;23(1):241-246.
119. Schieda N, Kielar AZ, Al Dandan O, McInnes MD, Flood TA. Ten uncommon and unusual variants of renal angiomyolipoma (AML): Radiologic-pathologic correlation. Clin Radiol. 2015;70(2):206-220.
120. Katabathina VS, Vikram R, Nagar AM, Tamboli P, Menias CO, Prasad SR. Mesenchymal neoplasms of the kidney in adults: Imaging spectrum with radiologic-pathologic correlation. Radiographics. 2010;30(6):1525-1540.
121. Milner J, McNeil B, Alioto J, Proud K, Rubinas T, Picken M, et al. Fat poor renal angiomyolipoma: Patient, computerized tomography and histological findings. J Urol. 2006;176(3):905-909.
122. Lee-Felker SA, Felker ER, Tan N, Margolis DJ, Young JR, Sayre J, et al. Qualitative and quantitative MDCT features for differentiating clear cell renal cell carcinoma from other solid renal cortical masses. AJR Am J Roentgenol. 2014;203(5):W516-W524.
123. Hindman N, Ngo L, Genega EM, Melamed J, Wei J, Braza JM, et al. Angiomyolipoma with minimal fat: Can it be differentiated from clear cell renal cell carcinoma by using standard MR techniques? Radiology. 2012;265(2): 468-477.
124. Amin MB, Crotty TB, Tickoo SK, Farrow GM. Renal oncocytoma: A reappraisal of morphologic features with clinicopathologic findings in 80 cases. Am J Surg Pathol. 1997;21(1):1-12.
125. Gudbjartsson T, Hardarson S, Petursdottir V, Thoroddsen A, Magnusson J, Einarsson GV. Renal oncocytoma: A clinicopathological analysis of 45 consecutive cases. BJU Int. 2005;96(9):1275-1279.
126. Dechet CB, Bostwick DG, Blute ML, Bryant SC, Zincke H. Renal oncocytoma: Multifocality, bilateralism, metachronous tumor development and coexistent renal cell carcinoma. J Urol. 1999;162(1):40-42.

127. Rosenkrantz AB, Hindman N, Fitzgerald EF, Niver BE, Melamed J, Babb JS. MRI features of renal oncocytoma and chromophobe renal cell carcinoma. AJR Am J Roentgenol. 2010;195(6):W421-W427.
128. Wu J, Zhu Q, Zhu W, Chen W, Wang S. Comparative study of CT appearances in renal oncocytoma and chromophobe renal cell carcinoma. Acta Radiol. 2016;57(4):500-506.
129. Woo S, Cho JY, Kim SH, Kim SY, Lee HJ, Hwang SI, et al. Segmental enhancement inversion of small renal oncocytoma: Differences in prevalence according to tumor size. AJR Am J Roentgenol. 2013;200(5):1054-1059.
130. Ganeshan D, Iyer R, Devine C, Bhosale P, Paulson E. Imaging of primary and secondary renal lymphoma. AJR Am J Roentgenol. 2013;201(5):W712-W719.
131. Sheth S, Ali S, Fishman E. Imaging of renal lymphoma: Patterns of disease with pathologic correlation. Radiographics. 2006;26(4):1151-1168.
132. El-Sharkawy MS, Siddiqui N, Aleem A, Diab AA. Renal involvement in lymphoma: Prevalence and various patterns of involvement on abdominal CT. Int Urol Nephrol. 2007;39(3):929-933.
133. Nguyen DD, Rakita D. Renal lymphoma: MR appearance with diffusion-weighted imaging. J Comput Assist Tomogr. 2013;37(5):840-842.
134. Prando A, Prando D, Prando P. Renal cell carcinoma: Unusual imaging manifestations. Radiographics. 2006;26(1):233-244.
135. Mendhiratta N, Muraki P, Sisk AE Jr, Shuch B. Papillary renal cell carcinoma: Review. Urol Oncol. 2021;39(6):327-337.
136. Mitsufuji T, Fujimitsu R, Ida M, Urakawa H, Kora S, Takeshita M, et al. Papillary renal cell carcinoma with extensive paraaortic nodal metastasis mimicking malignant lymphoma. Magn Reson Med Sci. 2011;10(3):201-204.
137. Streiff MB. Thrombosis in the setting of cancer. Hematology Am Soc Hematol Educ Program. 2016;2016(1):196-205.
138. Cassell A, Jalloh M, Yunusa B, Ndoye M, Mbodji MM, Diallo A, et al. Management of renal cell carcinoma-current practice in Sub-Saharan Africa. J Kidney Cancer VHL. 2019;6(2):1-9.
139. Coulibaly MT, Sissoko I, Berthé A, Amadou BI, Traore ML, Ouattara Z. Management of kidney cancers in Urology Department of the Gabriel Toure University Hospital/ Bamako. Surg Sci. 2018;9(06):183.
140. Muhammed A, LawalAhmad LT, MaitamaHussaini Y, Abdullahi S, Ahmad B, Liman AA. Pathologic characteristics and management of renal cell carcinoma in Zaria, Nigeria. Sub-Saharan Afr J Med. 2015;2(1):1.
141. Salako AA, Badmus TA, Badmos RA, David A, Laoye A, Akinbolaet IA, et al. Renal cell carcinoma in a semi-urban population of south-western Nigeria. East Afr Med J. 2017;94(1):37-43.
142. Farber NJ, Kim CJ, Modi PK, Hon JD, Sadimin ET, Singer EA. Renal cell carcinoma: The search for a reliable biomarker. Transl Cancer Res. 2017;6(3):620-632.
143. Raina P, Singh SK, Goswami AK, Kashyap MK, Khullar M, Sharma SK, et al. MN/CA9 gene expression as a potential tumor marker for renal cell carcinoma. Mol Cell Biochem. 2022;477(2):333-343.
144. Gurel S, Narra V, Elsayes KM, Siegel CL, Chen ZE, Brown JJ. Subtypes of renal cell carcinoma: MRI and pathological features. Diagn Interv Radiol. 2013;19(4):304-311.
145. Pedrosa I, Chou MT, Ngo L, H Baroni R, Genega EM, Galaburda L, et al. MR classification of renal masses with pathologic correlation. Eur Radiol. 2008;18(2):365-375.
146. Pedrosa I, Alsop DC, Rofsky NM. Magnetic resonance imaging as a biomarker in renal cell carcinoma. Cancer. 2009;115(10):2334-2345.
147. Ren A, Cai F, Shang YN, Ma ES, Huang ZG, Wang W, et al. Differentiation of renal oncocytoma and renal clear cell carcinoma using relative CT enhancement ratio. Chin Med J (Engl). 2015;128(2):175-179.
148. Karlo CA, Donati OF, Burger IA, Zheng J, Moskowitz CS, Hricak H, et al. MR imaging of renal cortical tumours: Qualitative and quantitative chemical shift imaging parameters. Eur Radiol. 2013;23(6):1738-1744.
149. Park SB, Cho KS, Lee JH, Jeong YK, Choi SH, Kang BS, et al. Unusual manifestations of renal cell carcinoma. Acta Radiol. 2008;49(7):839-847.
150. Amin MB, Amin MB, Tamboli P, Javidan J, Stricker H, de-Peralta Venturina M, et al. Prognostic impact of histologic subtyping of adult renal epithelial neoplasms: An experience of 405 cases. Am J Surg Pathol. 2002;26(3):281-291.
151. Goyal A, Sharma R, Bhalla AS, Gamanagatti S, Seth A, Iyer VK, et al. Diffusion-weighted MRI in renal cell carcinoma: A surrogate marker for predicting nuclear grade and histological subtype. Acta Radiol. 2012;53(3):349-358.
152. Choi YA, Kim CK, Park SY, Cho SW, Park BK. Subtype differentiation of renal cell carcinoma using diffusion-weighted and blood oxygenation level-dependent MRI. AJR Am J Roentgenol. 2014;203(1):W78-W84.
153. Lassel EA, Rao R, Schwenke C, Schoenberg SO, Michaely HJ. Diffusion-weighted imaging of focal renal lesions: A meta-analysis. Eur Radiol. 2014;24(1):241-249.
154. Wang H, Cheng L, Zhang X, Wang D, Guo A, Gao Y, et al. Renal cell carcinoma: Diffusion-weighted MR imaging for subtype differentiation at 3.0 T. Radiology. 2010;257(1):135-143.
155. Young JR, Margolis D, Sauk S, Pantuck AJ, Sayre J, Raman SS. Clear cell renal cell carcinoma: Discrimination from other renal cell carcinoma subtypes and oncocytoma at multiphasic multidetector CT. Radiology. 2013;267(2):444-453.
156. Sun MR, Ngo L, Genega EM, Atkins MB, Finn ME, Rofsky NM, et al. Renal cell carcinoma: Dynamic contrast-enhanced MR imaging for differentiation of tumor subtypes--correlation with pathologic findings. Radiology. 2009;250(3):793-802.
157. Piscaglia F, Nolsøe C, Dietrich CF, Cosgrove DO, Gilja OH, Bachmann Nielsen M, et al. The EFSUMB Guidelines and Recommendations on the Clinical Practice of Contrast Enhanced Ultrasound (CEUS): Update 2011 on non-hepatic applications. Ultraschall Med. 2012;33(1):33-59.
158. Xue LY, Lu Q, Huang BJ, Ma JJ, Yan LX, Wen JX, et al. Contrast-enhanced ultrasonography for evaluation of cystic renal mass: In comparison to contrast-enhanced CT and conventional ultrasound. Abdom Imaging. 2014;39(6):1274-1283.
159. Reiner CS, Roessle M, Thiesler T, Eberli D, Klotz E, Frauenfelder T, et al. Computed tomography perfusion imaging of renal cell carcinoma: Systematic comparison with histopathological angiogenic and prognostic markers. Invest Radiol. 2013;48(4):183-191.

160. Das CJ, Thingujam U, Panda A, Sharma S, Gupta AK. Perfusion computed tomography in renal cell carcinoma. World J Radiol. 2015;7(7):170-179.
161. Nakajima R, Abe K, Kondo T, Tanabe K, Sakai S. Clinical role of early dynamic FDG-PET/CT for the evaluation of renal cell carcinoma. Eur Radiol. 2016;26(6):1852-1862.
162. Safaei A, Figlin R, Hoh CK, Silverman DH, Seltzer M, Phelps ME, et al. The usefulness of F-18 deoxyglucose whole-body positron emission tomography (PET) for re-staging of renal cell cancer. Clin Nephrol. 2002;57(1):56-62.
163. Nakatani K, Nakamoto Y, Saga T, Higashi T, Togashi K. The potential clinical value of FDG-PET for recurrent renal cell carcinoma. Eur J Radiol. 2011;79(1):29-35.
164. Tatar G, Gündoğan C, Şahin ÖF, Arslan E, Ergül N, Çermik TF. Prognostic significance of 18F-FDG PET/CT imaging in survival outcomes in patients with renal cell carcinoma. Mol Imaging Radionucl Ther. 2022;31(3):200-206.
165. Alongi P, Picchio M, Zattoni F, Spallino M, Gianolli L, Saladini G, et al. Recurrent renal cell carcinoma: Clinical and prognostic value of FDG PET/CT. Eur J Nucl Med Mol Imaging. 2016;43(3):464-473.
166. Lindenberg L, Mena E, Choyke PL, Bouchelouche K. PET imaging in renal cancer. Curr Opin Oncol. 2019;31(3):216-221.
167. Hirasawa H, Taketomi-Takahashi A, Katsumata N, Higuchi T, Sekine Y, Suzuki K, et al. Efficacy of 18F-fluorodeoxyglucose positron emission tomography/computed tomography for detecting renal cell carcinoma in patients with end-stage renal disease. Jpn J Radiol. 2024;42(10):1178-1186.
168. Murphy WM, Zambroni BR, Emerson LD, Moinuddin S, Lee LH. Aspiration biopsy of the kidney: Simultaneous collection of cytological and histological specimens. Cancer. 1985;56:200-205.
169. Sahni VA, Silverman SG. Biopsy of renal masses: When and why. Cancer Imaging. 2009;9(1):44-55.
170. Lim CS, Schieda N, Silverman SG. Update on indications for percutaneous renal mass biopsy in the era of advanced CT and MRI. AJR Am J Roentgenol. 2019;212(6):1187-1196.
171. Zhou M, Roma A, Magi-Galluzi C. The usefulness of immunohistochemical markers in the differential diagnosis of renal neoplasms. Clin Lab Med. 2005;25:247-257.
172. Habas E, Akbar R, Farfar K, Arrayes N, Habas A, Rayani A, et al. Malignancy diseases and kidneys: A nephrologist prospect and updated review. Medicine (Baltimore). 2023;102(15):e33505.
173. Capitanio U, Volpe A. Renal tumor biopsy: More dogma belied. Eur Urol. 2015;68(6):1014-1015.
174. Canvasser NE, Kay FU, Xi Y, Pinho DF, Costa D, de Leon AD, et al. Diagnostic accuracy of multiparametric magnetic resonance imaging to identify clear cell renal cell carcinoma in cT1a renal masses. J Urol. 2017;198(4):780-786.
175. Kay FU, Canvasser NE, Xi Y, Pinho DF, Costa DN, Diaz de Leon A, et al. Diagnostic performance and interreader agreement of a standardized MR imaging approach in the prediction of small renal mass histology. Radiology. 2018;287(2):543-553.
176. Chiarello MA, Mali RD, Kang SK. Diagnostic accuracy of MRI for detection of papillary renal cell carcinoma: A systematic review and meta-analysis. AJR Am J Roentgenol. 2018;211(4):812-821.
177. Lim RS, Flood TA, McInnes MDF, Lavallee LT, Schieda N. Renal angiomyolipoma without visible fat: Can we make the diagnosis using CT and MRI? Eur Radiol. 2018;28(2):542-553.
178. Vargas HA, Delaney HG, Delappe EM, Wang Y, Zheng J, Moskowitz CS, et al. Multiphasic contrast-enhanced MRI: Single-slice versus volumetric quantification of tumor enhancement for the assessment of renal clear-cell carcinoma Fuhrman grade. J Magn Reson Imaging. 2013;37(5):1160-1167.
179. Vendrami CL, Velichko YS, Miller FH, Chatterjee A, Villavicencio CP, Yaghmai V, et al. Differentiation of papillary renal cell carcinoma subtypes on MRI: Qualitative and texture analysis. AJR Am J Roentgenol. 2018;211(6):1234-1245.
180. Schieda N, Lim RS, Krishna S, McInnes MDF, Flood TA, Thornhill RE. Diagnostic accuracy of unenhanced CT analysis to differentiate low-grade from high-grade chromophobe renal cell carcinoma. AJR Am J Roentgenol. 2018;210(5):1079-1087.
181. Chen K, Lee BL, Huang HH, Tan BY, Lee LS, Ng LG, et al. Tumor size and Fuhrman grade further enhance the prognostic impact of perinephric fat invasion and renal vein extension in T3a staging of renal cell carcinoma. Int J Urol. 2017;24(1):51-58.
182. Fontenil A, Bigot P, Bernhard JC, Beauval JB, Soulié M, Charles T, et al. Who is dying after nephrectomy for cancer? Study of risk factors and causes of death after analyzing morbidity and mortality reviews (UroCCR-33 study). Prog Urol. 2019;29(5):282-287.
183. Uzzo RG, Novick AC. Nephron sparing surgery for renal tumors: Indications, techniques and outcomes. J Urol. 2001;166(1):6-18.
184. Ljungberg B, Albiges L, Abu-Ghanem Y, Bedke J, Capitanio U, Dabestani S, et al. European Association of Urology Guidelines on Renal Cell Carcinoma: The 2022 Update. Eur Urol. 2022;82(4):399-410.
185. Huang WC, Levey AS, Serio AM, Snyder M, Vickers AJ, Raj GV, et al. Chronic kidney disease after nephrectomy in patients with renal cortical tumours: A retrospective cohort study. Lancet Oncol. 2006;7(9):735-740.
186. Yildirim H, Schuurman MS, Widdershoven CV, Lagerveld BW, van den Brink L, Ruiter AEC, et al. Variation in the management of cT1 renal cancer by surgical hospital volume: A nationwide study. BJUI Compass. 2023;4(4):455-463.
187. Tengue K, Kpatcha TM, Sonhaye L. Cancer du rein de l'Adulte au Togo: Fréquence, diagnostic, traitement et évolution. Rev Afr Urol Androl. 2015;1(4):177-182.
188. Tijani KH, Anunobi CC, Ezenwa EV, Lawal A, Habeebu MYM, Jejeet EA, et al. Adult renal cell carcinoma in Lagos: Experience and challenges at the Lagos University Teaching Hospital. African J Urol. 2012;18(1):20-23.
189. Motzer RJ, Agarwal N, Beard C, Bolger GB, Boston B, Carducci MA, et al.; National Comprehensive Cancer Network. Kidney cancer. J Natl Compr Canc Netw. 2011;9(9):960-977.
190. Flanigan RC, Mickisch G, Sylvester R, Tangen C, Van Poppel H, Crawford ED. Cytoreductive nephrectomy in patients with metastatic renal cancer: A combined analysis. J Urol. 2004;171(3):1071-1076.
191. Ferriero M, Cacciatore L, Ochoa M, Mastroianni R, Tuderti G, Costantini M, et al. The impact of metastasectomy on

survival outcomes of renal cell carcinoma: A 10-year single center experience. Cancers (Basel). 2023;15(13):3332.
192. Rendon RA, Kapoor A, Breau R, Leveridge M, Feifer A, Black PC, et al. Surgical management of renal cell carcinoma: Canadian kidney cancer forum consensus. Can Urol Assoc J. 2014;8(5-6):E398.
193. Deleuze A, Saout J, Dugay F, Peyronnet B, Mathieu R, Verhoest G, et al. Immunotherapy in renal cell carcinoma: The future is now. Int J Mol Sci. 2020;21(7):2532.
194. Rini BI, Plimack ER, Stus V, Gafanov R, Hawkins R, Nosov D, et al. Pembrolizumab plus Axitinib versus Sunitinib for advanced renal-cell carcinoma. N Engl J Med. 2019;380(12):1116-1127.
195. Plimack ER, Powles T, Stus V, Gafanov R, Nosov D, Waddell T, et al. Pembrolizumab plus Axitinib versus Sunitinib as first-line treatment of advanced renal cell carcinoma: 43-month follow-up of the phase 3 KEYNOTE-426 study. Eur Urol. 2023;84(5):449-454.
196. Canales Rojas R. Update on immunotherapy for renal cancer. Medwave. 2021;21(5):e8202.
197. Han Y, Liu D, Li L. PD-1/PD-L1 pathway: Current researches in cancer. Am J Cancer Res. 2020;10(3):727-742.
198. Motzer RJ, Rini BI, McDermott DF, Aren Frontera O, Hammers HJ, Carducci MA, et al. Nivolumab plus ipilimumab versus sunitinib in first-line treatment for advanced renal cell carcinoma: Extended follow-up of efficacy and safety results from a randomised, controlled, phase 3 trial. Lancet Oncol. 2019;20(10):1370-1385.
199. Rini BI, Powles T, Atkins MB, Escudier B, McDermott DF, Suarez C, et al. Atezolizumab plus bevacizumab versus sunitinib in patients with previously untreated metastatic renal cell carcinoma (IMmotion151): A multicentre, open-label, phase 3, randomised controlled trial. Lancet. 2019;393(10189):2404-2415.
200. Sepe P, Mennitto A, Corti F PG. Immunotherapeutic targets and therapy for renal cell carcinoma. Immunotargets Ther. 2020;9:273-288.
201. Choueiri TK, Motzer RJ, Rini BI, Haanen JB, Campbell MT, Venkatakrishnan K, et al. Updated efficacy results from the JAVELIN Renal 101 trial: First-line avelumab plus axitinib versus sunitinib in patients with advanced renal cell carcinoma. Ann Oncol. 2020;31(8):1030-1039.
202. Van Praet C, Slots C, Vasdev N, Rottey S, Fonteyne V, Andras I, et al. Current role of cytoreductive nephrectomy in metastatic renal cell carcinoma. Turk J Urol. 2021; 47(Suppl 1):S79-S84.
203. Bex A, Albiges L, Ljungberg B, Mulders P, Powles T, Staehler M, et al. Position of cytoreductive nephrectomy in the setting of metastatic renal cell carcinoma patients: Does the CARMENA trial lead to a paradigm shift? Eur Urol. 2019;75(1):111-113.
204. Van Poppel H, Jonas U, Kirchhoff TD, Mickisch GH, Zattoni F, Schröder FH, et al. Cytoreductive nephrectomy in the era of targeted therapies: A review. BJU Int. 2017;120(1):125-129.
205. Mejean A, Ravaud A, Thezenas S, Colas S, Beauval JB, Bensalah K, et al. Sunitinib alone or after nephrectomy in metastatic renal-cell carcinoma. N Engl J Med. 2018;379(5):417-427.
206. Bex A, Mulders P, Jewett M, Wagstaff J, van Thienen JV, Blank CU, et al. Immediate versus deferred nephrectomy combined with sunitinib in patients with synchronous metastatic renal cell carcinoma (SURTIME): A randomized controlled trial. Lancet Oncol. 2019;20(5): 647-659.
207. Bhindi B, Abel EJ, Albiges L, Bensalah K, Boorjian SA, Daneshmand S, et al. Systematic review of the role of cytoreductive nephrectomy in the targeted therapy era and beyond: An individualized approach to metastatic renal cell carcinoma. Eur Urol. 2019;75(1):111-128.
208. Motzer RJ, Jonasch E, Agarwal N, Beard C, Bhayani S, Bolger GB, et al. Kidney cancer, version 3.2015. J Natl Compr Canc Netw. 2015;13(2):151-159.
209. Mir MC, Derweesh I, Porpiglia F, Zargar H, Mottrie A, Autorino R. Partial nephrectomy versus radical nephrectomy for clinical T1b and T2 renal tumors: A systematic review and meta-analysis of comparative studies. Eur Urol. 2017;71(4):606-617.
210. Levy DA, Slaton JW, Swanson DA, Dinney CP. Stage specific guidelines for surveillance after radical nephrectomy for local renal cell carcinoma. J Urol. 1998;159(4):1163-1167.
211. Avakoudjo D, Hounnasso PP, Traore MT, Natchagandé G, Pare AK, Tore-Sanni R, et al. Experience with managing solid kidney tumours in Cotonou, Benin Republic. J West Afr Coll Surg. 2014;4(4):100-111.
212. Atanda AT, Haruna MS. Renal cell carcinoma in Nigeria: A systematic review. Sahel Med J. 2017;20(4):137.
213. Ahmed M, Oyelowo N, Bello AK, Lawal AT, Maitama HY, Khalifa A, et al. Peculiarities of renal cell carcinoma in young adults. Arch Int Surg. 2018;8:59-62.
214. Milonas D, Skulčius G, Baltrimavičius R, Auškalnis S, Kinčius M, Matjošaitis A, et al. Comparison of long-term results after nephron-sparing surgery and radical nephrectomy in treating 4- to 7-cm renal cell carcinoma. Medicina (Kaunas). 2013;49(5):223-228.