

# Onconephrology—Cancer and Kidney: Emerging Challenges in Management



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Received: 23 September 2025; Accepted: 13 October 2025

## ABSTRACT

Onconephrology is a new subspecialty that deals with the intersection between oncology and nephrology. The emergence of newer modalities of cancer therapy, although prolonging life, has had adverse effects on kidney function, either due to malignancy or as a side effect of treatment. One in nine Indians will likely develop cancer during their lifetime. India, with an overwhelming chronic kidney disease prevalence of 17.2%, is expected to face enormous challenges with cancer and concurrent kidney disease. Effective management requires a multidisciplinary approach that promotes collaboration between oncologists and nephrologists to enhance patient outcomes. Detailed history, physical examination, imaging, and other investigations, including tumor markers and kidney function monitoring, are mandatory for the management of individuals with cancer and acute and chronic kidney injury. This article highlights the importance of onconephrology in India.

*Journal of The Association of Physicians of India* (2026): 10.59556/japi.74.1498

## DEFINITION

Onconephrology is a new field in medicine that focuses on the intricate connections between cancer, its treatments, and renal disorders. In 2022, India recorded around 1,461,427 new cancer cases (crude rate: 100.4 per 100,000 individuals). One in nine Indians will probably develop cancer at some point in their lives. Lung cancer and breast cancer were the most prevalent cancers among men and women, respectively. According to estimates, the number of cancer cases will rise by 12.8% by 2025 compared to 2020.<sup>1</sup>

## THE IMPORTANCE OF ONCONEPHROLOGY

Onconephrology addresses the unique intersection of kidney disease and cancer, where renal complications can arise from tumors, therapies, or associated conditions. Kidney dysfunction affects treatment, quality of life, and survival, likely due to cardiovascular complications or drug dosage adjustments. For general physicians, understanding onconephrology is essential for its early detection, timely referral, and effective collaboration with specialists. Novel therapies for cancer treatment have improved the survival of patients with cancer. To individualize treatment, it is critical to identify individuals who are at high risk of developing adverse kidney outcomes. Many advances, including supportive care and kidney replacement therapy (dialysis), have improved the outcomes of critically ill patients. A multidisciplinary approach involving oncologists, renal physicians,

pharmacists, pathologists, internists, urologists, and intensive care physicians is important for the timely identification and management of these patients.

## ACUTE KIDNEY INJURY

Acute kidney injury is the most common cause of renal consultations in patients with cancer. Patients with cancer having a creatinine increase above 50% have a 17.5% 1-year risk of AKI, and their risk increases by 27% over five years.<sup>2</sup> The etiology of acute kidney injury in patients with cancer is multifactorial (Fig. 1). Acute renal injury is linked with higher death rates, can disrupt cancer treatment, potentially reduce treatment effectiveness, lead to treatment delays or interruptions, and can also lead to longer hospitalizations and increased healthcare costs. The in-hospital death rate from AKI is 15%, and there is a 48% probability that renal function will not recover.

## Drug- and therapy-associated AKI

### Chemotherapy-related

One of the most common and serious adverse effects of chemotherapeutic agents is AKI. Several factors influence the pathophysiology of chemotherapy-induced AKI: immune-mediated reactions, systemic hemodynamic changes, and direct nephrotoxic effects.

Commonly used platinum-based chemotherapeutic agents that cause kidney injury include cisplatin (20–30%), carboplatin (10–15%), and oxaliplatin (<5%). These agents also lead to electrolyte abnormalities, including hypomagnesemia, hyponatremia,

salt-wasting syndrome, hypokalemia, nephrogenic diabetes insipidus, distal renal tubular acidosis, and Fanconi syndrome. The administration of cisplatin, carboplatin, and pemetrexed was based on the creatinine clearance. If the GFR is < 45 mL/min, pemetrexed is contraindicated. Ifosfamide has been associated with proximal tubular dysfunction and AKI. Methotrexate precipitation and its metabolites in the tubular lumen result in AKI and crystalline nephropathy.<sup>3,4</sup>

## Targeted Therapies

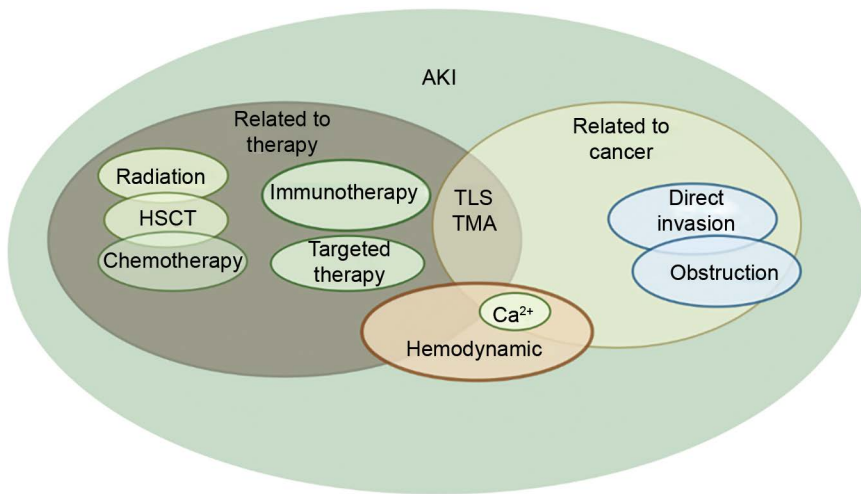
Recent advances in molecular targeted therapies have gradually advanced cancer treatment and improved survival. By modulating specific targets or receptors implicated in tumor growth and progression, these molecules prevent the growth of cancer. The majority of the targeted pathways are present in the renal system. Targeted therapies may result in toxicities ranging from asymptomatic proteinuria to kidney failure due to injury to the glomeruli, tubules, interstitium, or microvasculature.

## Inhibitors of Vascular Endothelial Growth Factor and its Receptors

Hypertension is one of the most common side effects of medications that inhibit the vascular endothelial growth factor (VEGF) pathway. The incidence varies between 30% and 80%, depending upon the individual medication, dosage, and concomitant diseases. Better survival may be correlated with the occurrence of class-defined adverse events during treatment, e.g., hypertension. Maintaining appropriate medication intensity

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**How to cite this article:** Keechilat P, Vijayan SN, Abraham G. Onconephrology—Cancer and Kidney: Emerging Challenges in Management. *J Assoc Physicians India* 2026;74(5):85–90.



**Fig. 1:** Acute kidney injury (AKI)-related to therapy and cancer

and guaranteeing therapeutic effectiveness relies on the prompt detection, prevention, and control of hypertension. Effective management of preexisting hypertension is crucial prior to initiating antiangiogenic therapy, and patients must get regular blood pressure assessments.  $\beta$ -blockers, dihydropyrimidine calcium channel blockers (CCB), angiotensin-converting enzyme inhibitors (ACEi), and angiotensin II receptor blockers (ARB) are among the first-line treatments for antiangiogenic-induced hypertension.<sup>5</sup> Avoid all nondihydropyridine calcium channel blockers (e.g., diltiazem, verapamil) during tyrosine kinase inhibitor therapy, as they inhibit TKI metabolism through cytochrome P450.

The most frequent adverse nephrological event was proteinuria. Because proteinuria is frequently minor and asymptomatic, it does not necessitate discontinuing medication or altering the dosage. The prevalence of nephrotic-range proteinuria (> 3 gm/day) occurs in about 1–5%. Treatment may have to be stopped if there is AKI, nephrotic syndrome, thrombotic microangiopathy, or symptomatic proteinuria (edema, weight gain, and pleural effusion). In such instances, medications may be restarted at reduced dosages or on an intermittent schedule following an improvement in the grade of proteinuria.<sup>5</sup> It is essential to regularly check for proteinuria and renal function before starting the treatment and at the end of each cycle. ACEIs and ARBs can also be used to manage proteinuria.

Imatinib may precipitate TLS, proximal tubular dysfunction, Fanconi syndrome, and toxic tubular injury by inhibiting platelet-derived growth factor, which is essential for tubular regeneration after acute tubular necrosis (ATN). AKI is seen in 5–7% and CKD in 12% of patients treated with imatinib.

Hypophosphatemia occurs in about 10% of patients.

#### Cyclin-dependent Kinase 4/6 Inhibitors

Patients taking *cyclin-dependent kinase 4/6* (CDK 4/6) inhibitors have a higher incidence of adverse nephrotoxic effects. Creatinine elevation occurs in 18% of individuals on CDK4/6 inhibitors. Relative risks of nephrotoxicity were 9.94 for abemaciclib, 1.59 for palbociclib, and 3.23 for ribociclib. The mechanism underlying the nephrotoxicity of CDK 4/6 inhibitors is unclear. Inhibition of tubular creatinine secretion is another mechanism by which CDK4/6i may lead to “pseudoacute kidney injury (pseudo-AKI)”. Pseudo-AKI is more commonly seen with abemaciclib. The measurement of cystatin C may avert unwarranted dosage modifications or stopping the drugs.<sup>6,7</sup>

#### Immune Checkpoint Inhibitors

The occurrence of AKI is less than 5% in individuals undergoing monotherapy with immune checkpoint inhibitors (ICIs), whereas the risk increases when dual ICIs [Programmed Cell Death Protein 1 and its ligand (PD1/PDL-1) and Cytotoxic T-lymphocyte Associated Protein 4 (CTLA-4)] are used or when used in conjunction with proton pump inhibitors, nonsteroidal anti-inflammatory medications, and antibiotics. The most prevalent pathology is acute tubulointerstitial nephritis (ATIN), followed by pauci-immune glomerulonephritis, podocytopathies such as minimal change disease, and C3 glomerulonephritis. Treatments include withholding ICIs, stopping ATIN-associated medications, and starting corticosteroids (if AKI is stage 2) or temporary dialysis. Most patients recover entirely or partially with these approaches, while a small minority require

additional immunosuppressive therapy (mycophenolate mofetil, azathioprine, cyclosporine, infliximab, cyclophosphamide, or rituximab).<sup>8,9</sup> In patients with stage 3 AKI, permanent discontinuation of ICI treatment is recommended. In less than 10% of cases, irreversible renal function loss may necessitate dialysis.

#### Chimeric antigen receptor (CAR)-modified T cells (CAR-Ts)

Chimeric antigen receptor-modified T cell (CAR-T)-associated cytokine release syndrome is the most important side effect resulting from rapid immune activation and the release of high levels of cytokines such as interleukin-6. Cytokine release syndrome initially presents with fever, which may progress to hypoxia, hypotension, and AKI. Cytokine release syndrome typically manifests within the first week following CAR-T cell infusion and reaches its peak between 1 and 2 weeks.

Cytokine release syndrome (CRS) prevention includes prior chemotherapy to reduce the tumor burden and steroids to suppress the effect of cytokines. Treatment includes the use of vasopressors, intravenous fluids, oxygen therapy, and, in severe cases, tocilizumab (IL-6 inhibitor) and/or steroids.<sup>10</sup>

#### Malignancy-associated AKI

##### Tumor Lysis Syndrome

Tumor lysis syndrome (TKS) is an oncological emergency characterized by hyperkalemia, hyperphosphatemia, hyperuricemia, and hypocalcemia, resulting from massive tumor cell lysis. The primary mechanisms in TLS contributing to AKI encompass renal artery vasoconstriction, compromised perfusion, deposition of uric acid, calcium, and phosphate in the tubules, as well as oxidative stress and inflammation of renal tissue.

Prophylactic measures include intravenous hydration and the maintenance of urine output to mitigate the risk of AKI. Individuals exhibiting severe TLS require continuous kidney replacement therapy with a higher dialysate flow.<sup>11</sup>

Bisphosphonates are used for hypercalcemia or bone metastases, and nephrotoxicity is dependent upon both dosage and duration of infusion. Renal toxicity can be avoided by monitoring serum creatinine levels prior to infusion and adjusting the doses based on the creatinine clearance (GFR). Intravenous zoledronic acid should be avoided in patients with GFR <35 mL/min.<sup>12</sup>

**Radiotherapy:** Radiation of the kidneys can lead to chronic interstitial fibrosis and CKD. The kidney damage caused by radiation has a

long latency period. It takes at least 6 months after radiation therapy to show signs of kidney dysfunction, and it could take years for the condition to progress to the point where it is clinically noticeable.

**Biomarkers for AKI:** Neutrophil gelatinase-associated lipocalin (NGAL), kidney injury molecule-1 (KIM-1), N-acetyl- $\beta$ -D-glucosaminidase (NAG), and liver-type fatty acid-binding protein (L-FABP) are examples of tubular injury markers that can detect AKI earlier than serum creatinine, which allows for early intervention.<sup>13</sup> Urinary C-X-C-motif ligand 9 (CXCL9) was helpful in distinguishing immune checkpoint inhibitor-associated acute interstitial nephritis (AIN) from alternative etiologies of AIN.<sup>14</sup>

**Direct tumor infiltration:** Lymphomas or leukemias infiltrate the renal parenchyma, causing proteinuria, hematuria, AKI, or CKD.

**Obstruction:** Tumors can obstruct the urinary tract and cause postrenal AKI. Pelvic tumors (e.g., prostate, cervical, or bladder cancer) or retroperitoneal lymphadenopathy compress the ureters, causing post-renal AKI.

### Multiple Myeloma

Approximately 50% of patients have a blood creatinine level  $\geq 2$  mg/dL at the time of initial diagnosis. Renal failure in MM is multifactorial, involving monoclonal immunoglobulin (Ig), tubular dysfunction (Fanconi syndrome), infection, and hypercalcemia. The mechanisms by which monoclonal immunoglobulins induce renal injury include intratubular precipitation (e.g., light chain cast nephropathy—LCCN), tissue deposition (e.g., monoclonal immunoglobulin deposition disease), fibrillogenesis (for example, AL amyloidosis), crystallization (e.g., crystalline light chain proximal tubulopathy), complement activation (e.g., C3 glomerulopathy associated with monoclonal gammopathy), and cytokine activation (e.g., POEMS syndrome).<sup>15</sup> Of this most prevalent renal lesion caused by multiple myeloma is LCCN. It is observed in 40–60% of renal biopsies in individuals with multiple myeloma and renal impairment. Renal impairment in patients with multiple myeloma is reversible in 20–60% of cases.

### Monoclonal Gammopathy of Renal Significance (MGRS)

The term “MGRS” refers to kidney lesions caused by a renal-toxic monoclonal protein that is generated by a clonal B cell or plasma cell that is not classified as a hematological neoplasm by the World Health Organization criteria. The most common MGRS condition is AL amyloidosis, which is linked to a greater risk of dying, likely due to systemic involvement

of the disease. Timely diagnosis is crucial in these patients. The diagnosis is confirmed via a combination of kidney biopsy and diagnostic work-up of the underlying clonal disorder.<sup>16</sup> In patients who have renal disease and monoclonal gammopathy, the Mayo MGRS Prediction Tool (available online [https://mdevans.shinyapps.io/mgrs\\_app/](https://mdevans.shinyapps.io/mgrs_app/)), which employs eight variables derived from blood and urine analysis parameters, aids clinicians in calculating the likelihood of detecting an MGRS lesion in a renal biopsy.<sup>17</sup> The therapeutic strategy is directed toward B-cell clones, plasma cell clones, or any identifiable monoclonal protein. Chemotherapy aimed at plasma cell or B-cell malignancies and autologous hematopoietic cell transplantation may be used to treat MGRS. Renal outcomes in patients with MGRS are strongly related to hematologic response to treatment.

### Thrombotic Microangiopathy

Thrombotic microangiopathy (TMA) is characterized by the development of microthrombi in small vessels and is caused by endothelial dysfunction, leading to organ damage. Three factors are associated with cancer-associated TMA (CA-TMA): chemotherapy (gemcitabine, proteasome inhibitors, VEGF inhibitors, and peptide receptor radionuclide therapy), active malignancy (mucin-producing gastric, lung, and breast cancers), and hematopoietic stem cell transplantation. CA-TMA is a rare condition that is associated with high mortality rates. In patients with cancer, VWF levels are high, and ADAMTS13 metalloproteinase activity is significantly reduced. In addition to increasing VWF levels and decreasing ADAMTS13 levels, chemotherapy increases the VWF/ADAMTS13 ratio, which increases the risk of thrombosis. The treatment of TMA includes determining the underlying cause, suppressing complement activation, and managing complications with supportive care. Plasmapheresis may be helpful in treating TTP-like symptoms. Unlike TTP, CA-TMA usually does not respond to plasma exchange (PEX), and the only therapy to improve mortality and mitigate organ damage is chemotherapy. Prompt diagnosis and treatment are essential in improving the outcomes.<sup>18</sup>

### Paraneoplastic Glomerular Diseases (PGD)

Of adult cancer patients with overt renal symptoms, fewer than 1% develop PGD.

Membranous nephropathy (MN) is a common complication.

In some cases, PGD may be the initial presentation prior to the diagnosis of

malignancy. Clinicians should consider malignancies in patients with recent renal issues and a documented history of cancer, especially in older adults. Most cases are immunologically mediated. The primary treatment is controlling the underlying malignancy, which will result in improvement of glomerular dysfunction.<sup>19,20</sup>

## ELECTROLYTE IMBALANCES IN CANCER PATIENTS

### Hyponatremia

The most prevalent electrolyte imbalance among hospitalized cancer patients is hyponatremia, which is associated with high death rates, prolonged hospitalizations, and increased treatment costs. Hyponatremia in patients with cancer is associated with reduced survival and a poor response to chemotherapy. The most common etiology of hyponatremia is the syndrome of inappropriate antidiuretic hormone secretion (SIADH). Common causes of SIADH are small-cell lung cancer and drugs such as cyclophosphamide, vinblastine, and vincristine. The mechanisms of cisplatin-induced hyponatremia include renal salt-wasting syndrome and SIADH. Other causes include adrenal insufficiency, chemotherapy-induced nausea and vomiting, and the administration of hypotonic intravenous fluids. The etiology and severity of hyponatremia dictate the course of treatment. Fluid restriction is challenging for patients with SIADH, particularly when chemotherapy is administered, and more hydration is frequently needed. It is possible to treat acute hyponatremia in the noncancer population immediately using hypertonic saline and salt pills over an extended period. Vasopressin receptor antagonists, such as tolvaptan, are also effective in correcting hyponatremia in cancer patients. It is essential to start tolvaptan at a lower dose (7.5 mg/day), especially in SCLC, and titrate up as needed to avoid overcorrection.<sup>21</sup>

### Cancer-related Hypercalcemia

The most frequent cause of hypercalcemia in hospitalized patients is malignancy. Patients with advanced cancer typically have hypercalcemia and a dismal prognosis. Malignancy-associated hypercalcemia is caused by (1) excessive secretion of parathyroid hormone-related protein (PTHrP) by various solid tumors, (2) bony metastases resulting in the release of osteoclast-activating factors, such as multiple myeloma and breast cancer, and (3) secretion of 1,25-dihydroxy vitamin D as in cases of lymphoma. Given that hypercalcemia of malignancy is associated with considerable morbidity and may have

a negative impact on a patient's quality of life, early detection and care treatment are important.

The definitive therapy for hypercalcemia of malignancy is the management of the underlying cancer. The acute management of hypercalcemia aims to lower calcium levels through hydration, enhance renal calcium excretion (via hydration and calcitonin), and reduce bone resorption (by using calcitonin, bisphosphonates, and denosumab). Calcitonin acts within 2–6 hours and decreases calcium levels by 1–2 mg/dL. Disadvantages include the rapid development of tachyphylaxis. It has been demonstrated that zoledronate is more effective than pamidronate in treating malignancy-associated hypercalcemia. Zoledronate's action starts in 48–72 hours, and a complete response occurs within 7–10 days.<sup>22</sup> Corticosteroids are useful for patients with increased 1,25-dihydroxy vitamin D production, as they reduce vitamin D production and decrease intestinal calcium absorption.

### Hyperkalemia

Hyperkalemia is most frequently associated with AKI, TLS, or obstructive nephropathy (also known as hyperkalemic or type 4 renal tubular acidosis), which may be a consequence of pseudohyperkalemia caused by severe leukocytosis or thrombocytosis. For accurate potassium measurements in this situation, it is useful to use plasma samples, and to reduce cell lysis, blood samples should be transported blood samples to the laboratory in an icebox to minimize cell lysis.

### Hypomagnesemia

Hypomagnesemia is a frequent electrolyte abnormality in cancer patients and is linked with drugs such as cisplatin and EGFR inhibitors. Magnesium plays a major role in many enzymatic reactions. Cetuximab, proton pump inhibitors, aminoglycoside antibiotics, calcineurin inhibitors, and amphotericin B. Cisplatin, cetuximab, panitumumab, and aminoglycosides cause hypomagnesemia due to renal losses. In the case of cisplatin, renal magnesium wasting continues for several months or even years after cessation of the drug. However, cetuximab-related hypomagnesemia is reversible. The treatment of hypomagnesemia should be determined based on the severity and cause of deficiency. Oral magnesium supplementation may be used in patients with mild asymptomatic hypomagnesemia. When a patient has symptomatic hypomagnesemia or severe hypomagnesemia (magnesium levels <0.5 mmol/L), intravenous (IV) magnesium supplementation is necessary.<sup>23</sup>

## CHRONIC KIDNEY DISEASE AND CANCER

Chronic kidney disease (CKD) is a frequent problem related to cancer and its treatment. Compared with people without CKD, cancer patients with CKD may be at an increased risk of death. It is currently unknown how common CKD is in cancer patients, although there is mounting evidence that the risk is significant and continues to rise. The chance of developing CKD depends on various factors, such as the type of malignancy—whether a solid or hematologic malignancy, history of nephrectomy or hematopoietic stem cell transplant (HSCT), and the administration of nephrotoxic chemotherapy. Hemodialysis patients with end-stage kidney failure exhibit a greater prevalence of cancer compared to the general population. Approximately 50% of anticancer medications are eliminated in urine as either unaltered drugs or active metabolites. These medications require modification due to reduced renal clearance to prevent the build-up of harmful metabolites or medication overdose. A thorough examination of medications and polypharmacy is essential to prevent interactions between anticancer and other drugs.

KDIGO (Kidney Disease Improving Global Outcomes) recommends two simple screening tests: (1) serum creatinine and (2) urine albumin-to-creatinine ratio (UACR). The KDIGO heatmap categorizes CKD into four types based on eGFR and albuminuria. Low risk (in the absence of additional indicators of renal disease, no CKD)—green; moderately increased risk—yellow; high risk—orange, and very high risk—red. A UACR of > 30 mg/g or an eGFR of less than 60 mL/min/1.73 m<sup>2</sup>, persisting for three months or more, indicates chronic kidney disease. Additional findings, such as urine sediment abnormalities (hematuria, red cell casts) or small kidney size on renal ultrasonography, further support a diagnosis of CKD. According to the CKD "heatmap," increased UACR and decreased eGFR are typically linked to poor prognosis in CKD (Fig. 2).<sup>24</sup>

## WHEN TO REFER TO A NEPHROLOGIST

Current KDIGO guideline recommendations are as follows: unclear etiology of CKD; eGFR <30 mL/min/1.73 m<sup>2</sup>; sustained decline in GFR exceeding 20% or 30% in individuals commencing hemodynamically active therapies; substantial albuminuria (albumin-to-creatinine ratio (ACR) ≥300 mg/g or protein-to-creatinine ratio (PCR) ≥500 mg/g)

concomitant with hematuria; ≥2-fold elevation in albuminuria in individuals with significant albuminuria under surveillance; unexplained and persistent urinary red blood cell casts, red blood cells (RBC) >20 per high-power field, and CKD with hypertension unresponsive to ≥4 antihypertensive agents.<sup>24</sup>

## ROLE OF NEPHROPATHOLOGIST

### Renal Pathology in Oncology: Diagnostic and Clinical Relevance

Renal dysfunction in patients with cancer results from various causes, such as systemic anticancer therapies, paraneoplastic syndromes, radiation-related injury, opportunistic infections, direct tumor infiltration, or obstructive uropathy. Each mechanism is associated with specific histopathological characteristics, requiring thorough assessment through light microscopy (LM), immunofluorescence (IF), and electron microscopy (EM). The KDIGO 2024 Chronic Kidney Disease Guidelines emphasize that kidney biopsy is an acceptable, safe, and clinically valuable diagnostic tool for elucidating the underlying cause of kidney disease and guiding therapeutic decision-making when appropriate.<sup>24</sup>

Glomerular diseases associated with malignancy include membranous nephropathy, minimal change disease, IgA nephropathy, IgA vasculitis nephritis, pauci-immune crescentic glomerulonephritis (GN), membranoproliferative GN, and renal amyloidosis. These entities may precede, coexist with, or recur during the course of malignancy, highlighting the necessity for careful clinicopathological correlation. Membranous nephropathy is a typical example of cancer-associated glomerulopathy. Recent advances have identified target antigens, including thrombospondin type-1 domain-containing 7A (THSD7A) and neural epidermal growth factor-like protein 1 (NELL1), in glomerular immune deposits, providing mechanistic insights into tumor-related immune dysregulation.<sup>25</sup>

Monoclonal gammopathy-related kidney disease is another critical consideration. In several cases, renal biopsy with IF studies provides the first evidence of nephrotoxic monoclonal protein deposition, often detected during evaluation for otherwise unexplained chronic kidney disease. Biopsy is indispensable for therapy-related renal injury. For example, more than half of thrombotic microangiopathy (TMA) cases secondary to VEGF inhibitors are localized to the kidney, underscoring the necessity for tissue diagnosis.<sup>26</sup> Moreover, proteinuria

KDIGO: Prognosis of CKD by GFR and albuminuria categories				Albuminuria categories Description and range		
				A1	A2	A13
				Normal or mildly increased	Moderately increased	Severely increased
				UACR <30 mg/g	UACR 30-300 mg/g	UACR >300 mg/g
GFR categories (mL/min/1.73 m <sup>2</sup> ) Description and range	G1	Normal or high	≥90			
	G2	Mildly decreased	60–89			
	G3a	Mildly to moderately decreased	45–59			
	G3b	Moderately to severely decreased	30–44			
	G34	Severely decreased	15–29			
	G35	Kidney failure	<15			

**Fig. 2:** KDIGO heatmap illustrating the prognosis of CKD based on categories of eGFR and albuminuria [Green—low risk (if no other markers of kidney disease, no CKD); Yellow—moderately increased risk; Orange—high risk; Red—very high risk]

linked to anti-VEGF therapy, even if mild and without evident renal dysfunction, may indicate clinically relevant histopathological damage. Proteinuria may indicate treatment toxicity and could also represent paraneoplastic membranous nephropathy, necessitating therapy intensification instead of discontinuation.<sup>26</sup>

Nephrologists play a crucial role in the multidisciplinary management of cancer patients experiencing renal dysfunction. In addition to establishing a precise histopathological diagnosis, they provide prognostic information by evaluating activity and chronicity indices in the glomerular, tubulointerstitial, and vascular compartments, which is crucial for customizing oncologic and nephrological treatments, informing choices regarding renal replacement therapy, and predicting the likelihood of renal recovery. The integration of nephropathology into oncology practice is essential to optimize patient outcomes in the context of targeted therapies, ICIs, and precision medicine. Administration of cytotoxic chemotherapy in patients receiving dialysis

The Onconephrotoxin Library Collaboration (OLIC) was launched online in 2022 (<https://www.olic-app.info/items-1-1>). It was created by a group of nephrologists, pathologists, and pharmacists,

in collaboration with the American Society of Onconephrology (ASON). The goal is to raise knowledge of possible side effects and interactions, as well as suggestions on how various chemotherapeutic medicines should be managed in dialysis patients.<sup>27</sup>

### CANCER TREATMENT IN INDIVIDUALS WITH IMPAIRED RENAL FUNCTION

To obtain the best clinical results, anticancer drugs must be correctly administered. Therefore, estimating kidney function is an essential part of the dosage process. Underestimating kidney function will lead to dose reduction and decreased efficacy, treatment failure, adoption of second- or third-line medications that are less effective or more toxic, and, eventually, a lower survival rate.<sup>28</sup> However, overestimation of kidney function leads to higher toxicity. The Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) formula performed better than other creatinine-based GFR estimation formulas in both cancer and noncancer populations and should be used to determine kidney function for drug dosing.

The 2021 CKD-EPI creatinine and cystatin levels are best for GFR assessment in patients with hematologic and solid cancers.<sup>29</sup>

### TRANSPLANT ONCONEPHROLOGY

Patients with chronic renal illness exhibit an increased risk of cancer and cancer-related mortality after transplantation. Kidney transplant recipients face a two-to threefold increased chance of developing cancer and dying from cancer relative to the general population. Most of the heightened risk is attributable to viral-mediated malignancies, including post-transplant lymphoproliferative disease, anogenital tumors, and Kaposi sarcoma. Nonmelanoma skin cancer is the most common malignancy among recipients of a kidney transplant. Both immunological and nonimmune factors predispose patients to cancer development after kidney transplantation, including age at transplantation, sex, ethnicity, duration of dialysis, history of malignancy, sun exposure, and virus exposure. Recipients of kidney transplants must adhere to age-appropriate cancer-screening protocols and implement preventive strategies against the most common solid organ malignancies.<sup>30</sup>

Physicians should monitor patients with cancer proactively (perform kidney function tests, electrolytes, and urine analysis in routine cancer patient follow-ups, especially during nephrotoxic treatments), recognize red flags such as rapid decline in eGFR, proteinuria, hematuria, or severe electrolyte imbalances, and refer to onconephrologists. Patients should be made aware of hydration and avoid the use of nephrotoxic drugs (for example, NSAIDs, aminoglycosides, and alternative drugs) and adhere to monitoring schedules.

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