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PhD THESIS

**CHRONIC KIDNEY DISEASE IN NEOPLASIA-KIDNEY
BETWEEN THE AFFLICTED AND THE AGGRESSOR**

A B S T R A C T

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ABSTRACT

I. INTRODUCTION

Chronic kidney disease is one of the leading risk factors for cancer and a significant health concern worldwide. Simultaneously, cancer, one of the most complex diseases of this century, characterized by its uncontrolled growth and spread of abnormal cells in the human body, appears to have, at least for now, an unbreakable link to chronic kidney disease.

Over time, this pathology has preoccupied the scientific community and all around the world, and even in our country researchers try to highlight the fact that the two diseases are interconnected by the risks and factors associated with CKD that increase the possibility of eventually developing cancer. At the same time, cancer itself can cause CKD either directly or indirectly, with both afflictions having a troubling connection.

Cancer is, without a doubt, one of the leading causes of morbidity and mortality, and the rate of new cases continues to rise every day. For patients with CKD, cancer is considered an added burden as it can be both the cause and the effect.

CKD, or chronic kidney disease, is an established risk factor and is characterized as kidney damage affecting more than 9.1% of the world's population. Patients with CKD are at higher risk of developing cancer, and the presence of CKD worsens the prognostic of cancer patients. Both conditions coexist and have a reciprocal relationship and this research topic is extremely important as worldwide there aren't enough studies that focus on the bond these conditions form together.

The mechanisms that determine the association between cancer and CKD can be multifactorial, as CKD may allow the existence of an environment that encourages cancer development.

The aim of our study is to emphasize the connection between CKD and cancer and the need for a multidisciplinary approach that is essential for optimizing patient outcomes. The thesis is consistent with current concerns at international and national level as both CKD and cancer are at the same time aggressors and afflictions.

The research focuses on patients from Timisoara, Romania but our findings can have a bigger relevance, as both afflictions continue to affect many people worldwide. The main objectives of this research are to analyze the complicated relationship between CKD and cancer and to identify the consequences these two pathologies can eventually have for patients. As the two conditions continue to evolve, we consider that an understanding of their dynamic becomes increasingly important.

The thesis is structured in two main sections, the general section and the special part, which includes an in-depth literature review, a detailed description of the methodology we used, a presentation, and a discussion of the obtained results.

II. GENERAL PART

CANCER: COMPLEX CONDITION AND AGGRESSOR.

The oldest description of cancer (although this name was not used) is contained in the Edwin Smith Papyrus dating from 3000 BC (in which 8 cases of breast tumors /ulcers were described). The origin of the word cancer is attributed to Hippocrates (460-370 BC), who used the terms "carcinos" and carcinoma to describe non-forming or ulcer-forming tumors. Later, Celsius (28-50 BC) translated the Greek term cancer, the Latin name for crab, and Galen (130-200 BC) used the term "oncos" (swelling in Greek) to describe tumors.

Cancer is characterized by the uncontrolled growth and spread of abnormal cells in the human body, which is composed of trillions of cells. Normally, cells grow, divide, and form new cells in an orderly manner to meet the needs of the organism. It covers a diverse spectrum of pathologies affecting different anatomical areas of the human body and is the second leading cause of death globally.

The spectrum of cancer types exceeds 100 distinct tumors, mainly referred to according to the anatomical location of origin or the histological cell type of origin. Cancer can be classified into six major categories based on the type of tissue cell it originates from carcinoma, sarcoma, myeloma, leukemia, lymphoma, and mixed types. In the medical diagnosis of cancer, it is important to categorize different tumor types into specific categories based on their origin.

Cancer remains one of the leading causes of morbidity and mortality worldwide. The global burden of cancer continues to rise, with an estimated 19.3

million new cases and 10 million cancer-related deaths in 2020. By 2040, the number of new cancer cases is expected to increase to 28.4 million and cancer-related deaths to 16.3 million.

The incidence of frequently diagnosed cancers worldwide was: female breast cancer 2.26 million cases (11.7%), lung cancer 2.21 million (11.4%), and prostate cancer 1.41 million (7.3%). According to the GLOBOCAN 2020 report, in Romania, out of a total of 98,886 new cancer cases, the most frequent are colorectal cancer 12,938 (13.1%), lung 12,122 (12.3%), breast 12,085 (12.2%), prostate 8,055 (8.1%), and bladder 5,135 (5.2%). Cancer-related mortality rates in Romania are higher than the European average, partly due to late diagnosis and limited access to cancer care and treatment. It is predicted that cancer will become the leading cause of death in every country in the 21st century.

Globally, there are several factors that influence the growth and progression of cancer incidence. Viral infections, such as those caused by human papillomavirus (HPV), hepatitis B (HBV), and hepatitis C (HCV), are considered to be involved in the etiology of specific types of cancer, such as cervical and liver cancer. The main causes of mortality associated with cancer are attributed to known risk factors, including tobacco use, exposure to infectious agents, unhealthy dietary habits, excessive body weight, lack of physical activity, and alcohol consumption.

Cancer incidence varies greatly between regions and countries worldwide, influenced by the population structure, society, economy, and lifestyle of different regions and countries. Due to the desire to fight this affliction different cancer treatments have emerged over time.

Cancer therapy has varied in terms of its effectiveness, resulting from a combination of hope for total remission and cure in some cases, and on the other hand, the ineffectiveness of treatments and the occurrence of side effects.

The three most commonly used cancer therapies are chemotherapy, surgery, and radiation therapy. Recent advances in oncology have led to a better understanding of the biological mechanisms underlying cancerous tissues, the identification of new therapeutic targets, and the development of innovative treatments that have the ability to address tumor specificity and minimize toxicity to healthy tissues.

The choice of the best cancer treatment option is influenced by several factors, including the type and stage of cancer, the health status of the patient, and the available treatment methods.

In recent years there have been significant advancements regarding cancer treatments. These include stem cell therapy, targeted therapy, ablation therapy, nanoparticles, natural antioxidants, radionics, chemodynamic therapy, sonodynamic therapy, and ferroptosis-based therapy. Oncology is currently focused on developing safe and effective cancer nanomedicines. Stem cell therapy has shown promising results in regenerating and repairing damaged tissues by targeting both primary and metastatic cancer foci. Nanoparticles have also opened new diagnostic and therapeutic options.

Cancer treatments have been improving for many years, unfortunately these improvements have yet to bring a solution to the numerous side effects. Even though researchers and scientists have constantly tried to minimize as much as possible the effects of cancer treatments it appears that for some diseases this sustained effort has to continue, one of these afflictions being chronic kidney disease.

CHRONIC KIDNEY DISEASE: AGGRESSOR AND PATHOLOGY

According to KDOQI criteria, CKD is characterized as kidney damage and/or a glomerular filtration rate (GFR) of 60 mL/min/1.73 m or less for three months or more.⁸⁵ GFR was measured with the Modification of Diet in Renal Disease (MDRD) equation based on serum creatinine levels.

Chronic kidney disease (CKD) is a global health problem affecting approximately 9.1% of the world's population. The prevalence of CKD differs by region, age, and sex, with higher rates in older people and among men. The leading causes of CKD include diabetes, hypertension and glomerular diseases. CKD is associated with an increased risk of morbidity and mortality, particularly due to cardiovascular complications and chronic end-stage kidney disease.

The prevalence of CKD in different regions of the world varies depending on demographics, genetics, lifestyle, and access to health care. In North America, the prevalence of CKD is about 14.2% in the United States and 12.5% in Canada.⁸⁹ In Europe, the prevalence varies between countries, with about 13% in the UK, 9.5% in Germany, and 15.1% in Spain. In Asia, the prevalence is about 17.2% in India and

8.2% in South Korea. In Latin America, the prevalence is about 7.1% overall, with 8.9% in Mexico and 9.2% in Brazil.

At the local level, the prevalence of CKD may vary depending on factors such as the age distribution of the population, the prevalence of diabetes and hypertension, the quality of medical care, and access to treatment. Studies show that CKD is more common among older people, men, and people with a genetic predisposition or family history of CKD.

In recent years, the prevalence of CKD has increased worldwide and locally, partly due to the ageing population and the increasing prevalence of risk factors such as diabetes and high blood pressure.⁸⁹ Improved access to health care and advances in the treatment of CKD have also contributed to the increase in the number of patients diagnosed with this condition.

The prevention and treatment of CKD locally and globally involve a multidisciplinary approach that includes identifying and controlling modifiable risk factors such as diabetes and hypertension, promoting a healthy lifestyle, and improving access to healthcare.

Data from the Romanian Renal Registry indicate that at the end of 2019, 16,326 patients received renal replacement therapy (RRT), with 14,111 on hemodialysis and 344 on peritoneal dialysis, approximately 1,871 with a kidney transplant. Geographically, the distribution of patients initiating RRT in Romania was uneven, with higher coverage around university centres and certain counties, also the cause of CKD remained unknown, highlighting the need for public health programs and the development of a specialized outpatient nephrology care network in Romania.

We can easily see that CKD is a complex disease, thus it has a high probability of forming a bond to an even more complex affliction which is cancer, both having the ability to lead to and result from each other.

CKD AND CANCER: AN INTER-CONNECTED BOND

Due to the increase in the number of new cancer cases over the years and life expectancy in neoplasia patients, we should also consider the increase in CKD prevalence among these patients. There are several mechanisms implied in kidney damage in the presence of neoplasia.

In the face of the life expectancy increase over the last decades and the fact that cancer is a chronic condition with a higher incidence at higher ages, patients with neoplasia have several characteristics that influence the prevalence of CKD. They tend to be older and present several comorbidities (arterial hypertension, diabetes mellitus, cardiovascular disease, liver disease, heart failure, etc.). All of these factors increase the prevalence of CKD. In the general population, the CKD prevalence is around 11% worldwide and increases up to 23 % in patients older than 75 years.

In the last 20 years, several published articles proved that patients with CKD after renal transplantation or on a form of renal replacement therapy are at higher risk of developing neoplasia. The presence of CKD worsens the prognostic of cancer patients. CKD can be associated with an increased risk of death from liver (74% higher risk), kidney (330% higher risk) and urinary tract cancer (730% higher risk).

Most of the published data report an increased cancer-related mortality in patients with CKD. Patients with CKD are already at an increased risk of death, most likely due to cardiovascular disease. The presence of chronic inflammation, the accumulation of uremic toxins and the relative state of immunosuppression contribute both to increased risk of neoplasia development and neoplasia-associated death.

As previously mentioned, there have been significant advancements regarding cancer treatments, but a number of antineoplastic agents are cleared by the kidney and may affect their function.

For example, many chemotherapy drugs are nephrotoxic, the kidney injuries they cause can range from acute kidney injury (AKI) to chronic kidney disease (CKD). Targeted therapies have revolutionized cancer treatment and generally have a better safety profile compared to traditional chemotherapeutic agents. However, they can still cause nephrotoxic effects: immune checkpoint inhibitors can lead to acute interstitial nephritis and AKI (acute kidney injury).

Contrast nephropathy, also known as contrast-induced nephropathy (CIN), is a significant concern in patients with neoplastic pathologies undergoing contrast-enhanced imaging procedures. The use of iodinated contrast agents in diagnostic imaging poses a potential risk to renal function, particularly in individuals with pre-existing renal impairment.

Contrast-enhanced CT scans are widely used to diagnose, stage, monitor, and evaluate the response to cancer therapy. However, cancer patients undergoing multiple scans may experience complications such as impaired renal function.

Radiation and Bone-Targeted Therapies can cause radiation nephritis, a form of kidney injury, and nephrotoxicity can be a limiting factor in treatments such as somatostatin receptor targeting peptide receptor radionuclide therapy and prostate-specific membrane antigen radioligand therapy, where the radiopharmaceutical is retained in the kidneys.

The complicated connection that CKD and cancer form accentuates the necessity for a field that helps in determining the risks or benefits of cancer treatments for patients that also have CKD.

ONCO-NEPHROLOGY: A CRUCIAL FIELD FOR CANCER AND CKD

Onco-Nephrology plays a very important role in the care and management of patients with both cancer and chronic kidney disease (CKD). The importance of Onco-Nephrology in this patient population can be highlighted in several key aspects: Patients with CKD are more susceptible to developing cancer and may require specialized care to manage both conditions effectively. Onco-Nephrology provides expertise in identifying and diagnosing kidney diseases in cancer patients, allowing for early intervention and appropriate management to prevent further kidney damage.

The overall aim of onco-nephrology is to assist cancer teams in identifying, treating, and, if possible, preventing kidney problems. Onco-Nephrology helps in assessing the risks and benefits of cancer treatments in the context of CKD, allowing for personalized treatment plans that optimize cancer outcomes while minimizing the potential harm to renal function.

ACUTE INJURY VS. CHRONIC DISEASE IN ONCOLOGIC PATIENTS

Kidney disease, whether acute or chronic, is a collection of intricate conditions that can be caused by or contribute to cancer. Chemotherapeutic agents, in particular, can lead to kidney disease. Unfortunately, many of the cancer chemotherapeutic agents currently in use, as well as those still in development, can

cause damage to the kidneys. This can result in impaired kidney function, which often becomes apparent during the final stages of cancer.

Acute kidney injury is a potential risk associated with cancer. This can be caused by various factors, such as urinary tract obstruction resulting from prostate or urothelial cancer, uterus or ovary cancer, retroperitoneal node enlargement, tumour mass, or retroperitoneal fibrosis. Other possible causes include infiltration of the kidney by renal cancer or lymphoma, glomerular or tubular diseases, and hypercalcemia.

The main focus of the general part is to show the correlation between CKD and cancer and to highlight the fact that a better understanding of these afflictions that become aggressors is of help for both nephrologists and oncologists.

III. SPECIAL PART

In this part of the thesis we analyzed four case studies, that show the interplay between neoplasia and kidney is at many levels.

In the first study, we performed a retrospective analysis on a large database from a hospital in the western part of Romania. We included more than 5000 patients in our analysis and showed that CKD incidence (stages G3-G5) is higher compared to general population and also that after one year of neoplasia evolution this incidence increases. Also, we identified the neoplasias that present the highest incidence of CKD. At the same time, we identified that an important part of the CKD patients required introduction of a form of renal-replacement therapy.

The cohort consisted of 5831 cancer patients who received a biopsy diagnosis at the largest oncology hospital and outpatient clinic in the region between January 2019 and December 2020. The study design followed an observational retrospective cohort approach.

All patients included in the study underwent various cancer treatments, including chemotherapy, radiotherapy, and/or surgery, either prior to or after their inclusion in the database.

In our database, the prevalence of CKD varied among different cancer types: breast, lung, colonic and prostate cancer. Besides the patient-specific and treatment-specific risk factors for CKD, there are also cancer-specific risk factors that can influence the incidence/prevalence of CKD. The prevalence of CKD was significantly

higher than the average prevalence in 13 of the cancer groups, with renal cancers and urothelial cancers showing statistically significant differences. Conversely, the prevalence of CKD was lower than the average in 10 of the cancer groups, but statistically significant differences were found only in colonic cancer and brain tumor patients.

In our region, the highest absolute number of CKD patients was observed among breast, lung, and prostate cancer patients. In fact, these three cancer types accounted for more than two-thirds of all CKD cases in our database. The prevalence of CKD varied depending on the age of the patients and the type of cancer.

Importantly, certain cancer types (including renal, urinary tract, pharyngeal, pancreatic, prostatic, uterus, and lung cancers) were associated with a significantly increased risk of developing CKD, even after adjusting for age and gender.

Surprisingly, the prevalence of advanced CKD stages (G4-G5-PD) was found to be remarkably high, accounting for 22.15% of cases. Notably, approximately one-third of the G5-Pre Dialysis patients had indications for initiating renal replacement therapy.

We concluded that given the substantial number of CKD cases among cancer patients, our findings suggest that the optimal management of these individuals should involve the collaboration of a nephrologist in addition to the primary oncology team.

In the second study, we analysed the rapid decline of estimated glomerular filtration rate and its effect on mortality risk of patients with hepatocellular carcinoma. In order to address this issue, we conducted a retrospective cohort study on more than 100 patients with a specific form of cancer, hepatocellular carcinoma respectively, who underwent percutaneous injection therapy. We evaluated the prevalence and determinants of rapid decline in kidney function and its impact on survival.

This study aimed to assess the rate of decline in renal function, identify factors associated with a rapid decline in renal function, and examine the relationship between rapid decline in estimated glomerular filtration rate (eGFR) and mortality in patients with hepatocellular carcinoma (HCC) who received percutaneous ethanol injection therapy (PEIT).

This prospective observational study included 114 consecutive patients with HCC related to hepatotropic viruses (HCV, HBV, and HBV/HCV coinfection) who

were admitted to the Department of Gastroenterology and Hepatology in Timisoara between January 2000 and December 2015. The patients were followed up until death or the end of the study period (December 31, 2015).

The findings demonstrated that almost half of HCC patients exhibited a rapid eGFR decline, which is significantly higher than data observed in the general population, where a rapid decline in kidney function is seen in only 16% of individuals.

Interestingly, in our study, patients with rapid eGFR decline had a higher baseline eGFR compared to those in the non-rapid eGFR decline group. This observation aligns with similar findings reported in both diabetic patients and the general population. The association between a higher baseline eGFR and a rapid decline in renal function may be attributed to structural damage within the glomeruli caused by persistent hemodynamic changes, such as vasodilation in afferent arterioles and vasoconstriction in efferent arterioles

This study presents several strengths: it is the first to establish an association between rapid declines in renal function and increased mortality risk in HCC patients. Additionally, the study highlights an independent association between the severity of HCC, as evaluated by the CLIP score, and the rapid decline in kidney function. The study emphasizes the crucial link between a swift decrease in eGFR (glomerular filtration rate) and a higher mortality rate, underscoring the need for early detection of HCC patients who are susceptible to rapid kidney function decline.

In the third study we analysed the impact of chronic kidney disease on the mortality rates of patients with urological cancers. The main objective of our study was to analyze the impact of

CKD on the overall mortality of patients diagnosed with the most frequent types of urological cancers. We chose our patients from a pool of 5831 newly diagnosed cancer patients in total, who were seen in a large oncology hospital and outpatient department in western Romania over a two-year period (1 January 2019–31 December 2020).

Every patient received cancer treatment, either prior to or following their analysis's inclusion. These treatments included ablative surgery, radiation, hormone therapy, chemotherapy, and immunotherapy. We separated the patients into two groups: the first group consisted of patients with CKD, and the second group (control

group) consisted of patients without CKD. This division was based on the baseline evaluation of renal function carried out at the time of the initial oncological diagnosis.

Prostate, bladder, and kidney cancers are the three most common urological cancers. The high mortality rates for all three urological malignancies observed in our study could be explained by the high incidence of CKD, the relatively high proportion of patients diagnosed in advanced stages (62.5% for prostate cancer, 45% for bladder cancer, 36% for renal cancer), the presence of significant concomitant cardiovascular disease and the specific situations encountered during the COVID-19 pandemic, when the follow-up, and therapy of some patients was significantly delayed.

We established that optimizing treatment decisions and management strategies can be achieved through close collaboration among urologists, oncologists, radiation therapy specialists, and nephrologists. Furthermore, as a member of the oncological multidisciplinary team, the abilities of a skilled nephrologist are crucial for the prevention, early detection, long-term follow-up, and targeted therapy of CKD in this patient population

In the fourth study, we examined how cancer manifests before and after the start of hemodialysis and its association with mortality. This is the first study investigating the spectrum of cancer and its association with mortality in a large Eastern European cohort of 1377 ESKD patients undergoing HD, representing 12.4% of the patients from The Romanian Renal Registry.

Cancer was diagnosed before HD initiation in 3.63% of the patients, and 6.89% of the patients developed cancer after HD initiation. Patients with "de novo" cancer after HD initiation were significantly older than those without cancer.

The study underscores the significant interrelation between cancer and chronic kidney disease (CKD) in Eastern European patients undergoing hemodialysis (HD). The findings reveal that the gastrointestinal and urinary tracts are primary cancer sites in this population, with a high prevalence of de novo cancers. Cancer risk is notably linked to older age and chronic tubulointerstitial nephritis (CTIN) as the cause of end-stage kidney disease (ESKD). Prior to HD, the most common cancer types were digestive and hematological.

Cancer significantly elevates all-cause mortality in patients on HD, with those having de novo cancers experiencing notably lower survival rates. This highlights the importance of establishing local cancer screening programs for ESKD patients on

HD. In the context of urological cancer, CKD emerges as a crucial predictor of mortality and prognosis, necessitating consideration in treatment planning.

Additionally, the study highlights the rapid decline in kidney function and its association with increased mortality in hepatocellular carcinoma (HCC) patients undergoing percutaneous ethanol injection therapy (PEIT).

This finding emphasizes the need for early detection of HCC patients at risk of rapid kidney function decline.

We determined the coexistence of cancer and CKD in patients, especially those undergoing HD, necessitates an integrated, multidisciplinary approach to care involving both oncologists and nephrologists.

IV. FINAL CONCLUSIONS

It's unequivocal that cancer and chronic kidney disease (CKD) connect and manifest in various ways. We showed in this thesis that cancer stands as a prominent cause of morbidity and mortality on a global scale and for individuals with CKD cancer is an additional threat, being both a potential cause and consequence of their condition.

CKD and cancer coexist and form a reciprocal relationship, CKD significantly impacting the prognosis of cancer patients. Research on this topic is crucial, as there is a notable scarcity of global studies focusing on the intricate connection between these two conditions.

The first part of this study emphasizes that neoplasia associated mortality increases in the presence of CKD, with CKD being linked to a higher risk of death from cancers affecting the liver, kidney, and urinary tract. The mechanisms underpinning the association between cancer and CKD are multifactorial. CKD may create an environment conducive to cancer development.

The intricate interplay between cancer and CKD necessitates a comprehensive approach from both oncologists and nephrologists for effective care and management. The troubling bond between these two conditions was highlighted throughout the four studies we conducted.

Considering the fact that in Romania cancer mortality rates are higher than the European average, partly due to late diagnosis, limited access to cancer care

and treatment, research on this topic is important mostly due to lack of scientific studies. Using this as a starting point we aimed to publish four studies.

After analysing a large cancer database from western Romania our research revealed a significantly higher prevalence of chronic kidney disease (CKD) in cancer patients compared to the general population. The prevalence of CKD varied depending on different factors. One of studies highlighted the significant interrelation between cancer and chronic kidney disease (CKD) in Eastern European patients undergoing hemodialysis (HD). The findings reveal that the gastrointestinal and urinary tracts are primary cancer sites in this population, with a high prevalence of de novo cancers. Cancer risk is notably linked to older age and chronic tubulointerstitial nephritis (CTIN) as the cause of end-stage kidney disease (ESKD). Prior to HD, the most common cancer types are digestive and hematological.

Cancer significantly elevates all-cause mortality in patients on HD, with those having de novo cancers experiencing notably lower survival rates. This highlights the importance of establishing local cancer screening programs for ESKD patients on HD. In the context of urological cancer, CKD emerges as a crucial predictor of mortality and prognosis, necessitating consideration in treatment planning.

The advancement of more effective cancer treatments, which may be nephrotoxic, has increased patient survival rates. However, this necessitates careful management and coordination among urologists, oncologists, radiation therapists, and nephrologists. The role of a skilled nephrologist is pivotal in the oncological multidisciplinary team for the prevention, early detection, follow-up, and targeted therapy of CKD in cancer patients.

Our second study highlights the rapid decline in kidney function and its association with increased mortality in hepatocellular carcinoma (HCC) patients undergoing percutaneous ethanol injection therapy (PEIT). This finding emphasizes the need for early detection of HCC patients at risk of rapid kidney function decline.

Our third analysis of a large cancer database in western Romania showed a significantly higher prevalence of CKD in cancer patients compared to the general population, particularly in renal and urothelial cancer patients. The prevalence of advanced CKD stages (G4-G5) was remarkably high, with a notable proportion of patients needing renal replacement therapy. Certain cancer types (including renal, urinary tract, pharyngeal, pancreatic, prostatic, uterus, and lung cancers) were

associated with a significantly increased risk of developing CKD, even after adjusting for age and gender.

Additionally, our fourth study showed that when determining the best course of cancer treatment, CKD should be taken into account as it is a strong predictor of the overall mortality and prognosis in urological cancer. The percentage of patients who survive longer thanks to the development of newer, more effective cancer treatments has increased, though unfortunately many of these treatments can be nephrotoxic. Optimizing treatment decisions and management strategies can be achieved through close collaboration among urologists, oncologists, radiation therapy specialists, and nephrologists. Furthermore, as a member of the oncological multidisciplinary team, the abilities of a skilled nephrologist are crucial for the prevention, early detection, long-term follow-up, and targeted therapy of CKD in this patient population.

In conclusion, all four studies reiterate that the coexistence of cancer and CKD in patients, necessitates an integrated, multidisciplinary approach involving both oncologists and nephrologists. This approach is essential for optimizing patient outcomes and addressing the unique challenges posed by the intersection of these two conditions.

An important step would be laying the foundation of a new subspecialty of onco-nephrology. This indispensable subspecialty helps in assessing the risks and benefits of cancer treatments in the context of CKD, allowing for personalized treatment plans that optimize cancer outcomes while minimizing the potential harm to renal function.