VILNIUS UNIVERSITY
MEDICAL FACULTY

The Final Thesis

"Dialysis in Patients with Cancer"

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2024

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Structure

1. Abstract

Cancer and chronic kidney disease (CKD) are prevalent global health challenges, often intersecting in clinical practice and complicating patient management. In 2020, an estimated 19.3 million new cancer cases and 10.0 million cancer-related deaths were reported worldwide, with lung cancer being the leading cause of cancer mortality. CKD affects 13.4% of the global population, with hemodialysis as the predominant treatment for end-stage renal disease. This review highlights the interplay between cancer and kidney disease, exploring the multifactorial etiologies of renal complications in cancer patients, including tumor-related factors, chemotherapy, and targeted therapies. Acute kidney injury, occurring in up to 29% of cancer patients, significantly impacts treatment outcomes and survival rates. The review underscores the importance of early detection, personalized dosing strategies, and multidisciplinary collaboration to optimize renal care in this population. Shared decision-making involving patients, caregivers, and healthcare providers is essential for navigating the complexities of treatment discontinuation and palliative care in advanced stages.

2. Keywords

kidney disease, end-stage renal disease, dialysis, cancer, cancer treatment, nephrotoxicity

3. Introduction

3.1. Cancer

Cancer arises from abnormal cell growth, triggered by various alterations in gene expression. These changes disrupt the delicate equilibrium between cell proliferation and death, culminating in the development of a cell population capable of invading tissues and spreading to remote locations. If left untreated, cancer can lead to significant health issues and ultimately, the demise of the host. The distinguishing features between malignant cancer and benign tumors lie in their capacity to locally invade, spread to nearby lymph nodes, and metastasize to distant organs within the body (1).

3.1.1. Cancer epidemiology

Worldwide, cancer is a major public health problem (2). In 2020 it accounted for an estimation of 19.3 million new cancer cases and 10.0 million cancer deaths (9.9 million excluding non-melanoma skin cancer) worldwide, with all cancers combined. The risk for the individual to get cancer during the lifetime before the age of 75 is about 20%. The risk of dying from the cancer is 10%. Female breast cancer became the most diagnosed cancer worldwide in 2020 with 2.26 million cases. Lung cancer was the second most diagnosed cancer with 2.21 million cases and caused by far the most cancer deaths (1.80 million deaths). Liver cancer caused 0.83 million and stomach cancer caused 0.77 million deaths (3).

In Germany almost 500.000 new cancer cases were estimated in 2020 (excluding non-melanoma skin cancer). 231.400 Women and 261.800 Men were diagnosed. Cancer in Women caused 104.949 deaths, in men 125.274 (excluding non-melanoma skin cancer). The most diagnosed cancer in Germany in 2020 was female breast cancer with an estimation of 70.550 new cases. Lung cancer was the second most diagnosed cancer with an estimation of 56.690 new cases, followed by Colon cancer with 54.770 new cases. By far the most cancer deaths were caused by lung cancer (44.817), followed by colon cancer (23.787) and female breast cancer (18.425) (4).

3.2. The Kidney

The kidney is a paired organ which is located near the spine at the level of the upper abdominal cavity. Together, both kidneys weigh around 300 grams and have a volume of 400 cubic centimetres (5).

It is undoubtedly one of the most important organs in the human body and fulfils numerous vital tasks. It controls and regulates the water and electrolyte balance, blood pressure and the acid-base balance. Furthermore, the kidney regulates blood pressure via various pathways, has important incretory functions with the formation of various hormones, such as erythropoietin or renin, and further controls bone mineralization (6).

Probably the best-known and most important function of the kidney is its ability to excrete metabolic waste products, foreign substances and toxins with the help of urine production and thus purify the blood (7). Kidney function can be determined using various parameters (8). In addition to albumin-creatinine ratio (ACR), urine sediment, electrolyte abnormality, histology and imaging, the glomerular filtration rate (GFR), which measures the amount of purified blood (in ml) per minute is considered an optimal way to determine kidney function (9). The GFR varies in healthy people and is usually between 120 and 90 (mL * min-1 based on 1.73 m2 body surface area) (10). The GFR is influenced by many factors. Medical or disease-specific factors (e.g. diabetes, hypertension, glomerulonephritis) are particularly important, as well as age (11). Albuminuria is equally important in the examination of kidney function. In healthy people, this is <10 mg/g urine (12).

3.2.1. Kidney disease

Kidney failure refers to the under function of one or both kidneys. As a result of kidney failure, the concentration of urinary substances (creatinine, urea, uric acid and others) in the blood increases. The difference between acute (N17 according to ICD-10) and chronic kidney failure (N18 according to ICD-10) lies primarily in the time component. Acute Kidney failure usually occurs suddenly and is often reversible within a short time. Chronic kidney failure is a continuously worsening disease. (13)

Therefore, the focus below is primarily on chronic kidney failure and the associated consequences. If kidney function is permanently reduced, it is referred to as chronic kidney disease (CKD). With a loss of around 80% of the nephrons, the kidney's functions can no longer be maintained. (14)

CKD is defined as a reduction of the GFR < 60 ml/min for 3 months or more, regardless of the cause or the presence of kidney damage (15). Patients with evidence of kidney damage on imaging, kidney biopsy, urine sediment abnormalities, electrolyte, or other abnormalities due to tubular disorders, history of kidney transplantation or albuminuria with an albumin excretion

rate (AER) ≥30mg/24 hours or an ACR of ≥30 mg/g for > 3 months also have kidney disease, even if the glomerular filtration rate is >60 ml/min. Patients without signs of kidney damage and a GFR >60 most likely do not have kidney disease (16). The CKD is divided into five stages according to the level of the glomerular filtration rate and three stages according to the albuminuria (Figure 1). (17)

Prognosis of CKD by GFR and Albuminuria Categories: KDIGO 2012

GFR categories (ml/min/ 1.73 m²) Description and range				Persistent albuminuria categories Description and range		
				A1	A2	A3
				Normal to mildly increased	Moderately increased	Severely increased
				<30 mg/g <3 mg/mmol	30-300 mg/g 3-30 mg/mmol	>300 mg/g >30 mg/mmol
	G1	Normal or high	≥90			
	G2	Mildly decreased	60-89			
	G3a	Mildly to moderately decreased	45-59			
	G3b	Moderately to severely decreased	30-44			
	G4	Severely decreased	15-29			
	G5	Kidney failure	<15			

Green: low risk (if no other markers of kidney disease, no CKD); Yellow: moderately increased risk; Orange: high risk; Red, very high risk.

Figure 1 Prognosis of CKD by GFR and Albuminuria Categories (KDIGO, 2012)

The severity of symptoms in kidney disease varies based on these stages. Initially, patients with chronic kidney disease may experience minimal or no symptoms, making early detection challenging. Diagnosis often occurs incidentally through laboratory abnormalities, such as elevated retention parameters, electrolyte fluctuations, or renal anemia. (18)

As the disease progresses, symptoms intensify, manifesting as signs of overhydration like hypertension and edema. Fatigue, reduced resilience, muscle cramps, and itching become prevalent. Disturbances in mineral balance may lead to renal osteopathy. In advanced stages, severe uremia can lead to nausea, vomiting, uremic pericarditis, and gastritis. In severe cases,

uremic encephalopathy can occur, presenting neurological symptoms and deficits, potentially leading to a coma. (19)

3.2.2. Treatment of kidney disease

The treatment approach for chronic renal disease focuses, like the treatment of acute renal disease, on two key aspects: the therapy of the underlying disease and the symptomatic therapy. Priority is given to treating the underlying disease cause, followed by efforts to prevent disease progression and manage secondary comorbidities such as renal anaemia and bone metabolism disorders. Renal-replacement therapy is considered as ultima ratio. Strategies to impede disease progression involve antihypertensive therapy, particularly with angiotensin-converting enzyme inhibitors, medication to reduce proteinuria, strict nicotine abstinence, and comprehensive vaccination protection. Additionally, screening for cardiovascular risk factors like hypercholesterolemia or metabolic syndrome is important because a reduction of the GFR poses as a significant risk factor for cardiovascular events. Managing metabolic acidosis and hyperkalaemia is essential. Similar to the treatment of acute kidney injury, adjustments in current medication are required to accommodate the reduced elimination capacity of the kidneys. (18,20,21)

3.2.3. Epidemiology of kidney disease

CKD often lacks noticeable symptoms until it reaches an advanced stage, making precise burden calculation challenging and prevalence data elusive (22).

In the USA, an observational Study indicated a rising prevalence from 10.8% to 13.1% between 1988-94 and 1999-2004. Coresh et al. account the ageing population and increase of prevalence of diabetes, hypertension and obesity for this increase (23). When defined solely by estimated GFR <60 ml/min, CKD prevalence ranges from 2.5% to 11.2% in Europe, North America, Asia and Australia according to James et al. 2010 (24).

A meta-analysis by Hill et al. 2016 of 100 studies with 6.908.440 patients estimated a global prevalence of CKD stages 1–5 at 13.4%, with stages 3–5 at 10.6%. The prevalence varied widely among the studies, with factors like diabetes, hypertension, and participant age strongly influenced the CKD prevalence. (25)

In Germany approximately 2.3% of people aged 18–79 years had an eGFR <60 ml/min. The prevalence increased with increasing age. Girnd et al. estimated that with subjects over 80 years

of age, who were not examined in the study, at least 2 million people in Germany are affected nationwide. Albuminuria ≥30 mg/l is present in 11.5% of the population. The study has shown that diabetes mellitus and arterial hypertension are important determinants for CKD like Coresh et al. assumed earlier. (26)

In the USA the number of newly registered end-stage renal disease (ESRD) patients rose from 97.856 to 134.837 between 2001 and 2019. 113.309 patients received in-center hemodialysis in 2021 initially. This represents 83.8% of the incident ESRD population. 17.236 patients received peritoneal dialysis (PD). This represents 12.7% of the incident ESRD population. For PD this is an increase of double the percentage of the 2008 PD receiving patients. The mean eGFR at the initiation of renal replacement therapy in 2021 was 9.9 ml/min. The overall mean hemoglobin level was 9.4 g/dl. (27)
In Germany in 2019 11.353 patients received dialysis initially. In total 93.089 patients were on dialysis. The highest prevalence was in the mean age of 71 (28).

3.3.Dialysis

The primary goals of renal replacement therapy are the removal of water and urinary substances like creatinine, urea, uremic toxins alongside the correction of electrolyte and acid-base balance disorders. The aim is to avoid complications associated with kidney disease. The dialysis indication for acute kidney disease is made if one of the following is present: therapy refractory anuria lasting more than twelve hours, an increase in serum creatinine above 1.0 mg/dl in 24 hours, hyperuricemia over 12 mg/dl, hyperkalaemia, metabolic acidosis, hyperhydration, symptoms of uraemia (nausea, vomiting, reduced performance, pruritus, pericarditis, encephalopathy), intoxication with dialyzable or ultra-filterable substances. The indication criteria for permanent dialysis are like those in the acute kidney disease, but in addition: therapy refractory arterial hypertension, peripheral and central oedemas due to hyperhydration, renal acidosis, renal anemia, GFR <7 ml/min. (19,20)

3.3.1. Types of dialysis

Hemodialysis (HD) is the most used dialysis procedure in Germany and the USA (28,29). Its objective is to reestablish intra- and extracellular fluid balance, to mimic normal kidney function. Urinary substances diffuse through a semipermeable membrane, permeable to molecules up to approximately 25,000 Daltons, into isotonic and isoionic dialysate fluid. The

concentration gradient between blood and dialysate is mechanically maintained. Additionally, if an osmotic or physical pressure gradient from blood to dialysate exists, ultrafiltration occurs, effectively removing water from the blood. To ensure accessible and repeatable vascular access, patients entering chronic intermittent dialysis programs, such as the Cimino-Shunt between the radial artery and cephalic vein, undergo the creation of an arteriovenous fistula. Chronic intermittent HD stands as the standard of care, predominantly performed in dialysis centers or, less commonly, as home dialysis. Research indicates that home dialysis yields lower morbidity and mortality rates, coupled with an enhanced quality of life. Home dialysis involves short or 8-hour sessions three times a week (20,30,31).

During HD therapy, potential side effects include hypotension, arising from significant fluid loss, as well as symptoms like nausea, vomiting, headaches, and muscle cramps. Rare but severe complications may include air embolism, hemolysis, or cardiac arrhythmias. Disequilibrium syndrome, resulting from the rapid elimination of osmotically active substances, can lead to cerebral edema due to a drop in osmotic intravascular pressure. Immediately post-dialysis, common complications involve drops in blood pressure and bleeding from the puncture sites. Beyond the dialysis session, hyperkalemia and peripheral or central edema may manifest, causing symptoms. Long-term consequences of HD encompass shunt infections, thrombotic events, ischemia, steal syndrome, and psychological issues. Additionally, increased vascular and cardiac pressure load, resulting from a direct connection between the arterial and venous systems without an intermediate capillary system, may lead to more frequent occurrences of aneurysms and heart failures. (20)
The prognosis for patients undergoing HD is age-dependent, with a 10-year survival rate of 55% that significantly decreases with advancing age (25).

The first continuous renal replacement therapy to be used, was arteriovenous hemofiltration (HF) in 1977. Hemofiltration (HF) differs from HD by not passing dialysis fluid through the dialyzer. Instead, an intravenous infusion of hemofiltration solution is introduced, which is then pushed through a hemofiltration membrane which extracts urinary substances from the blood. The pressure gradient is either formed by the natural pressure differences between the arterial and venous systems or is created artificially using a pump. The advantage is that larger molecules are also removed that cannot be eliminated as effectively with conventional HD. The renal replacement effect of HF is equivalent to HD and offers the advantage of lower circulatory strain. Hemofiltration is a continuous process, meaning it can be used over 24 hours.

Therefore, it is mainly used in the treatment of acute kidney injury (AKI) in intensive care. (19,20,32)

In hemodiafiltration (HDF), the two NEVs presented are combined. This results in good elimination of both low molecular weight (through diffusion) and medium molecular weight (through convective transport) urinary substances (20). There are currently no clear indication guidelines, but HDF is particularly beneficial for patients suffering from dialysis-related hypotension or who have a good overall prognosis but transplantation is ruled out or unlikely (33).

Peritoneal dialysis (PD) is another way to replicate kidney function. In this method, a dialysate is introduced into the abdominal cavity through a surgically inserted catheter. The exchange of substances and elimination of urinary substances occur along the peritoneum, acting as a semi-permeable membrane, employing diffusion, ultrafiltration, resorption, and mass transport. Similar to HD, various dialysates are available for peritoneal dialysis, allowing customization based on patient needs. (34)

PD can be performed on an outpatient basis without mechanical assistance, this known as continuous ambulatory PD (CAPD). Alternatively, mechanical methods are available on an outpatient basis, such as automated PD, continuously cyclic PD, or in a nocturnal intermittent PD setting. The advantage of nocturnal intermittent PD is reduced mobility restrictions during the day and cosmetic benefits, as patients are not burdened with a large abdominal volume of dialysate during daytime. (20,35)

Worldwide approximately 10% of dialysis patients in receive PD (20). Indications for PD align with those for HD and are particularly suitable for children, working and traveling patients, those facing challenges with HD therapy, and those desiring dietary flexibility (35).

While PD has no strict contraindications, good compliance with hygiene regulations during catheter use and regular outpatient check-ups are imperative. Contrary to past beliefs, there are now only relative contraindications, and the patient's suitability for the procedure must be assessed. Previous absolute contraindications, such as diverticulitis, have been reevaluated, making PD a viable option for many patients. (36)

Complications with PD may include infections related to the implanted catheter, peritonitis, hernias due to high abdominal pressure, and catheter obstructions or changes in position (34).

While PD is essentially an equivalent renal replacement therapy compared to HD, mortality rates differ, particularly in the initial years, influenced by patient age and pre-existing conditions. For instance, PD exhibits lower mortality than HD in younger patients, but this trend reverses with prolonged therapy duration. (20)

The “integrated care” concept involves initiating therapy with PD and later transitioning to HD. This approach offers advantages such as preserving remaining kidney function, minimizing cardiac stress, improving patient survival in the initial years of therapy, and safeguarding arm vessels for future HD shunt implantation (37). PD is considered a suitable option for every patient. Young patients without diabetes mellitus or prior cardiac illnesses benefit initially. As therapy duration increases, the disadvantages of PD become more pronounced, leading to a shift towards the benefits of HD, prompting a change in the chosen renal replacement method. (19,20)

4. Literature Selection Strategy

I searched in PubMed, ScienceDirect, Gelbe Liste and Google Scholar up to the beginning of April 2024 with the search terms “chronic kidney disease”, “chronic renal insufficiency”, “end stage renal disease”, “kidney disease” in combination with “treatment”, "dialysis" in combination with “epidemiology” or “withdrawal”, "cancer " in combination with “treatment” or “epidemiology” or "immune checkpoint inhibitors" or “kidney disease” or “treatment nephrotoxicity” or “kinase inhibitors” or “dosage adjustments” or “chemotherapy”, “tumor lysis syndrome”, additionally I searched the cancer therapeutics listed in the thesis by name.
I did not limit by language nor by date of the publication, but I selected publications largely from the last 10 years from journals with a high impact factor. For the epidemiological data I chose the latest possible publications. I also searched the reference lists of the articles identified by this search strategy and selected those i judged relevant. Review articles were included when they provided comprehensive overviews beyond the scope of this Review.

5. Cancer and kidney disease

Cancer and kidney disease are complex medical phenomena, the linking of which represents a relevant challenge in clinical practice. The kidneys play a central role in the maintenance of fluid and electrolyte balance and in the excretion of metabolic products. The prevalence of kidney disease associated with cancer varies depending on tumor type, stage and therapeutic interventions like chemotherapeutics, immune checkpoint inhibitors and tyrosine kinase inhibitors and surgery which may lead to tumor lysis syndrome or drug-induced nephropathy. Dehydration, sepsis, or contrast nephropathy can also occur. Certain types of cancer, especially kidney cancer, are directly associated with kidney complications due to multiple myeloma, urinary obstruction, or intravascular coagulation. (31,38)

In the table below, risk factors for acute kidney injury in cancer patients are listed (39).

Unalterable basic risks	**Acute risks or events**	**Risks due to nephrotoxicity**
• Age > 65 years • Female gender • Hypoalbuminemia Comorbidities: • Pre-existing CKD • Heart failure • Hypertension • Diabetes mellitus • Renal artery stenosis • Liver cirrhosis • Malignancy with high intrinsic risk of AKI	• Hypotension (Mean arterial pressure < 65 mmHg) • Sepsis • Volume depletion • Toxic cardiomyopathy • Electrolyte disturbances or hypercalcemia	• Contrast agents • Anti-infectives Medical concomitant therapy: • Diuretics • RAAS inhibitors • NSAIDs • Allopurinol

One of the prevalent and severe complications in treating cancer patients is acute kidney injury (AKI). This condition not only limits the ongoing cancer therapies but also amplifies toxicity, necessitating adjustments or alterations in chemotherapy regimens. Additionally, AKI often results in the exclusion of patients from participation in clinical trials. (39) AKI also is an important risk factor for the long-term development of CKD (40).

In the table below, different causes of CKD in cancer patients are listed (39).

Pre-existing renal insufficiency due to an existing kidney disease	• Diabetes and hypertension, which is the most common in pathogenesis and prevalence • Genetic kidney diseases • Acquired kidney diseases (e.g., glomerulonephritis, interstitial nephritis)
Renal insufficiency as a result of the malignant disease	• Renal insufficiency can be the leading symptom of an oncological disease • Myeloma • Lymphomas
Therapy-related renal insufficiency	• Medications (chemotherapy, inhibitors of intracellular signalling pathways) • Bone marrow transplant • Reduction of the renal parenchyma because of a Renal cell carcinoma • Loss of kidney mass due to radical surgical therapy, other tumors (e.g., colon, liver)

5.1. Prevalence of cancer-related kidney complications

According to a Danish study in which 37.267 tumor patients were followed for seven years, acute deterioration of kidney function was the most common comorbidity. The 1-year risk was 17.5%, 5.1% of these patients' required dialysis. The highest risk was associated with haematological neoplasms, particularly multiple myeloma. With these diseases, acute renal failure develops in approximately 60% of patients. (41)

Many chemotherapy drugs and cytotoxic drugs are excreted by the kidneys and can cause serious side effects in renal insufficiency if the dose is not adjusted. Patients with renal insufficiency also have a weakened immune system and may even be more susceptible to infectious complications. (42)

In recent years, also numerous targeted therapies have demonstrated notable efficacy and clinical advantages across various tumor types, leading to increased progression-free and

overall survivals. Immune checkpoint inhibitors became standard therapy over the last decade. Their efficacy is evident, among others they are used in cancers like melanoma, non-small cell lung cancer and microsatellite instability-high tumors. This group of medications is associated with an approximately four times increased risk of acute kidney damage, such as an increase in creatinine, acute tubulointerstitial nephritis or acute kidney failure. Patients who are receiving concurrent therapy with proton pump inhibitors, already have a pre-existing low GFR or experience extrarenal immune-related side effects are particularly at risk. A recent real-world study showed that 3.6% of 1,037 patients receiving ICI therapy developed immune-related acute kidney failure, with 22% of them already suffering from pre-existing chronic kidney disease. (38)

In a population of 2207 patients on immune checkpoint inhibitors, 25% developed AKI and their mortality was higher as well (43). In another study in which the most frequent malignancy was lung cancer, the most frequently prescribed checkpoint inhibitor was an anti-programmed death protein 1 antibody. 15.5% developed AKI. Garcia et al. also identified even one episode of AKI as an independent risk factor for mortality (44).

The IRMA studies (Insuffisance Rénale et Médicaments Anticancéreux - Renal Insufficiency and Anticancer Medications) in France reported a substantial prevalence of reduced GFR in cohorts of solid tumor patients, reaching 52.9% in IRMA-1 and 50.2% in IRMA-2. An additional high prevalence of stage 3–5 CKD (12.0% and 11.8%, respectively) was observed. Notably, the prevalence of CKD remained consistently high across various tumor types, including breast, colorectal, lung, ovarian, and prostate cancers. The IRMA studies included patients regardless of the disease pathology or treatment. (45,46)

Conversely, individuals with kidney disease face a higher incidence of cancers (47). It is indicated that men with at least stage 3 CKD have a significantly increased risk for cancer, particularly involving the lung and urinary tract, with a 29% increased risk for each 10-ml decline in estimated GFR. Additionally, Danish registry data showed a gradual rise in cancer prevalence among CKD patients, from 10.4% in 1993–2000 to 14.0% in 2001–2008, signalling a 35% increase. The most common cancers in this population included basal cell carcinoma, squamous-cell carcinoma of the skin, breast cancer, cancer of cervix uteri, melanoma, and cancers of the colon, respiratory tract, bladder, prostate. (48)

Lowrance et al. observed a population of 1.190.538 adults with no prior cancer. A low GFR was associated with renal and urothelial cancer (49).
In a Korean nationwide study, 48.315 patients on dialysis and controls were evaluated. It was observed that dialysis patients had an overall higher incidence of malignancy. The cancer risk was 1.54-fold higher. Colorectal, liver and stomach cancer were most common malignancies in the dialysis patient. (50)

6. Mechanisms leading to kidney complications in cancer

The reason for the high susceptibility of this organ is, on the one hand, the high blood flow rate in the kidney, approximately 25% of the cardiac output, which means that it is particularly exposed to foreign substances from the blood compared to other organs. In addition, the amount of a substance can be increased in relation to the systemic circulation due to concentration processes in the kidneys, reaching toxic levels. The kidney has numerous transport mechanisms through which substances from the primary urine can be reabsorbed and intracellular accumulation can occur. (18)

6.1. Nephrotoxicity of cancer therapies

Treatment with cancer drugs can lead to renal side effects. More conventional cancer treatments as well as more modern treatments can exhibit nephrotoxic potential. Among others examples for cytostatics are: cisplatin, methotrexate, ifosfamide, and gemcitabine. (51)

As stated earlier, standard cancer therapy nowadays includes immune checkpoint inhibitors, "Targeted therapies". In cancer there is usually a pathological overactivation of specific molecular signaling pathways of cell division or apoptosis inhibition. Targeted therapies specifically inhibit the growth or spread of tumor cells by directly intervening in the molecular signaling pathways. These signaling pathways are also present in many healthy body cells, including kidney cells, which is why undesirable renal side effects are not uncommon. In addition, these therapies are usually used for advanced or metastatic malignancies. Most patients have already undergone nephrotoxic therapies, as well as numerous imaging examinations with potentially nephrotoxic contrast agents and the kidneys may have already been damaged. (46,52,53)

In the IRMA studies, a notably high prevalence of kidney disease in cancer patients was observed. The anticancer medications administered to these patients, half of whom exhibit abnormal renal function, often require dosage adjustments due to reduced renal function and can potentially pose a risk of kidney toxicity in most cases. The reduced survival has been theorized to be associated with cardiovascular complications of kidney disease or could result from inadequate adjustments in drug dosage. (46)

6.1.1. Chemotherapeutics

6.1.1.1. Cisplatin

Cisplatin is a platin based cytostatic drug that is used to treat many different types of cancer, such as testicular, ovarian, bladder, squamous or small cell lung cancer (54).

It is suggested that once cisplatin is accumulated in the tubular cells, the effect is similar to the antineoplastic effect. These include Direct damage to the proximal tubules, leading to necrosis and apoptosis. Vascular damage as well, primarily caused by vasoconstriction in the framework of inflammatory reaction. An approximately 5x higher accumulation of cisplatin was found in proximal tubule cells than in blood plasma. (55,56)

Despite preventive measures, approximately one third of patients treated with cisplatin develop cisplatin nephrotoxicity, which is often the most important therapy-limiting factor. According to specialist information, cisplatin is contraindicated in renal insufficiency below a GFR of 60 ml/ml. (39,57)

Proper hydration and substitution of magnesium are key strategies to prevent AKI., The substitution of magnesium has proven to significantly lower the chances and intensity of cisplatin-related AKI, as highlighted in by Kidera et al. in 2014 (58).

Carboplatin, another platin based cytostatic, has reduced side effects in comparison to cisplatin. It is less nephrotoxic due to less renal clearance and it is rather used when the patient has a risk of AKI or already has CKD. (39)

6.1.1.2. Methotrexate

Methotrexate (MTX) is a cytostatic drug and is approved to treat leukaemia, breast cancer, lung cancer, head and neck cancers, sarcomas, lymphomas, and trophoblast tumors (59).

Crystal nephropathy stands out as the predominant cause of renal damage induced by methotrexate. The primary mechanism underlying MTX damage involves the formation of 7-hydroxy-methotrexate crystals, leading to toxic harm in the tubular system and subsequent

deterioration in kidney function, referred to as crystal nephropathy. This occurs due to the limited solubility of MTX in water under acidic conditions, with up to 80-90% of MTX being excreted unchanged in urine, promoting crystallization within the tubule system, and resulting in toxic consequences. According to Widemann, the occurrence of renal insufficiency was noted at 1.8% in osteosarcoma patients undergoing high-dose MTX therapy. (60)

The renal injury is typically reversible and non-oliguric, both high-dose and low-dose MTX treatments appear to contribute to a consistent decline in kidney function (61).

To mitigate kidney damage, vigilant monitoring of urine volume and urine pH is essential when encountering elevated MTX plasma levels and delayed renal excretion. Intensive fluid administration and urine alkalinization (pH > 7.0) play a crucial role. In cases where MTX plasma concentration surpasses toxic levels (>1 μM) and kidney function is compromised, the consideration of glucarpidase, a recombinant bacterial enzyme that converts MTX into water-soluble cleavage products, becomes relevant. (39)

6.1.1.3. Ifosfamide

Ifosfamide is an alkylating cytostatic agent and a cyclophosphamide isomer. It is used as to treat various types of cancer. Ifosfamide is used to treat diverse cancers, including, cervical, lymphoma, sarcoma, breast cancer, lung cancer and testicular tumors. Ifosfamide-induced kidney damage stems from direct toxicity affecting the proximal tubule. These effects can progress to the development of Fanconi syndrome, marked by glycosuria, tubular proteinuria, loss of amino acids and bicarbonate, along with a significant potassium deficiency. Alongside hypophosphatemia, there's a rare occurrence of polyuria leading to nephrogenic diabetes insipidus. Data are available mainly for pediatric and young adult patients. 30% of pediatric patients develop a mild kidney insuffiency. (39,62,63)

6.1.1.4. Gemcitabine

Gemcitabine is an antimetabolite cytostatic agent. It is used as chemotherapeutic for the following cancer types: testicular, breast, ovarian, non-small cell lung, pancreatic, and bladder. Gemcitabine is potentially nephrotoxic. Leal et al. 2014 observed a thrombotic microangiopathy in 1% of the gemcitabine treated patients. Clinically, increased arterial blood

pressure can be seen. Microangiopathic hemolytic anemia, thrombopenia and increased serum LDH is possible as well. (64,65)

Most common side effects of potentially nephrotoxic chemotherapeutics according to specialist information:

Chemotherapy	**Most common side effects (very common ≥ 1/10)**
Cisplatin (66)	• Nausea, vomiting (Most emetogenic drug among cytostatics) • Nephrotoxicity • Neurotoxicity (irreversible in 30-50% of cases) • Bone marrow suppression (leukopenia, thrombopenia, anaemia) • Ototoxicity
Carboplatin (67)	• Emesis, nausea; more common in patients previously treated with cisplatin myelosuppression • Renal dysfunction • Neurotoxicity
Ifosfamide (62)	• Nausea, vomiting • Myelosuppression • CNS toxicity • Nephrotoxicity and urotoxicity
Methotrexate (59)	• Myelosuppression (thrombopenia, leukopenia) • Gastrointestinal symptoms: stomatitis, vomiting, nausea • Increase in liver enzymes (GOT, GPT), AP, bilirubin • Deterioration in renal function with decrease in creatinine clearance
Gemcitabine (64)	• Myelosuppression (thrombopenia, neutropenia, anaemia) • Dyspnoea (usually mild and resolves quickly without treatment) • Emesis, nausea • Elevation of transaminases (GOT, GPT), alkaline phosphatase Haematuria, mild proteinuria

6.1.2. Immune checkpoint inhibitors

Approved checkpoint inhibitors, such as ipilimumab, nivolumab, pembrolizumab, atezolizumab, avelumab, and durvalumab, are increasingly used, this results in a rise in reports

of renal side effects. Immune checkpoint proteins are expressed on the surface of cancer cells which bind inhibitory T-cell receptors that deactivate T-cells. Checkpoint inhibitors inhibit those expressed proteins and allow the immune cells to identify and eliminate tumor cells. (68)

Depending on the surface-protein, checkpoint inhibitors can be organized to the following tagets: cytotoxic T-lymphocyte-associated protein 4 (CTLA-4), programmed cell death protein 1 (PD-1), and programmed death ligand 1 (PD-L1). While this drug-induced inhibition can enhance the immune system's control over tumors, it also poses a risk of disrupting self-tolerance and triggering immunological phenomena. (39)

Wanchoo et al. indicate an incidence of AKI in checkpoint inhibitor treated patients ranging from 1.7% to 6.7%. Some sources even suggest a probability of up to 14% for renal events associated with checkpoint inhibitors, and emerging data propose significantly higher AKI incidences (up to 29% for AKI stage 1 and 5-10% for AKI stage 2). These figures underscore the potential of renal toxicity linked to checkpoint inhibitors, particularly in combination therapies involving CTLA-4 and PD-1 inhibitors, which seem to pose an elevated risk of renal complications (39,69). In general, the timing of AKI onset during treatment seem to correlate with its severity. Typically, kidney function deterioration occurs between 21 and 245 days (median 91 days) after therapy initiation. PD-1 inhibitors like pembrolizumab tend to induce kidney injury within 3-10 months, while CTLA-4 inhibitors such as ipilimumab might lead to renal complications slightly earlier (usually within 2-3 months). Acute interstitial nephritis is the most common of kidney complication in patients on checkpoint inhibitors. Some cases exhibit granulomatous lesions, and there are rare reports of thrombotic microangiopathy or nephrotic syndrome development. Clinically, elevated serum creatinine and pyuria are evident in 68% of cases, with less frequent occurrences of eosinophilia (21%), haematuria (16%), or progressive arterial hypertonic blood pressure values (11%). Electrolyte disturbances, such as hyponatremia related to hypophysitis, have also been described for ipilimumab.
Both the PD-1 inhibitor pembrolizumab and nivolumab have been linked to renal rejection in kidney transplant patients with metastatic melanoma, particularly following prior therapy with CTLA-4 inhibitors. (39)

The American Society of Clinical Oncology (ASCO) has provided guidelines for managing renal complications with checkpoint inhibitors: For mild cases (grade 1 = AKI stage 1), a temporary interruption of therapy may be considered. In instances of moderate renal toxicity

(grade 2=ANV stage 2), a temporary treatment interruption is recommended, with the need to rule out other potential causes for AKI (such as contrast agents, other nephrotoxic drugs, or fluid status). Other potential causes for AKI, such as contrast agents, other nephrotoxic drugs, and fluid status, have been should have been excluded. The recommended course involves initiating therapy with prednisolone (0.5–1 mg/kg body weight or 1–2 mg/kg body weight if improvement is lacking). In severe cases like grade 3 or grade 4 which requires dialysis, a crucial aspect is the permanent avoidance of checkpoint inhibitors in therapy. Adhering to these guidelines results in approximately 80% of patients experiencing an improvement in kidney function, often with complete or at least partial normalization of kidney values. (70,71)

6.1.3. Kinase inhibitors

Kinases (phosphotransferases) are a large family of enzymes that are involved in the transmission and amplification of signals on and in cells. They exert their effects by phosphorylating their substrates. An uncontrolled activation of kinases can lead to cancer through the mutated kinase's ability to be ligand independent, this allows uncontrolled proliferation. Kinases are involved in the development, survival, new vessel formation and metastasis of tumors. (72)

The nephrotoxic effects associated with protein kinase inhibitor therapy vary among different substances but are generally less severe with single use, when combined with other nephrotoxic medications, these effects can become more pronounced. Commonly reported renal side effects include arterial hypertension, proteinuria, and electrolyte imbalances. Additionally, there have been reports of minimal change glomerulopathy, pauci-immune glomerulonephritis, and IgA glomerulonephritis linked to protein kinase inhibitor therapy. Arterial hypertension, proteinuria, or electrolyte disorders typically do not necessitate treatment interruption. Given that acute kidney function deterioration usually occurs within the initial months of therapy, vigilant monitoring of patients undergoing treatment, particularly in the post-initiation period, is advisable. (73)

Examples for potentially nephrotoxic kinase inhibitors are anaplastic-lymphomkinase-1 (ALK) Inhibitors (Crizotinib), BRAF-inhibitors (Dabrafenib, Vermurafenib), vascular endothelial growth factor (VEGF) Inhibitors (Bevacizumab, Aflibercept) and VEGF-receptor inhibitors (Sunitinib, Pazopanib, Axitinib) (39,72). In ALK inhibitor therapy, renal complications are

rather uncommon. Hypophosphatemia, hyponatraemia, hypokalaemia can occur as well as tubular damage. Temporarily reduced GFR was observed as well (74). In BRAF inhibitor therapy, acute interstitial nephritis can occur (75). During Dabrafenib and Trametinib therapy, nephrotic syndrome due to podocyte damage was observed in some cases (76). Proliferative glomerulonephritis with vasculitis can occur with Encorafenib and Binimetinib as therapeutic agent. Discontinuing of the BRAF inhibitor re-establishes the kidney function in 80% of cases (39,77). Glucocorticoid administration is sometimes prescribed to lower the serum creatinine (78).

In VEGF inhibitor therapy a typical complication is proteinuria, this is observed in 21-63% of cases. Severe proteinuria is observed in 6.5% of patients. Thrombotic microangiopathy changes can be seen as well as therapy refractory arterial hypertension. (79)

6.2. Tumor lysis syndrome

If the tumor breaks down quickly during treatment, or occasionally spontaneous, intracellular components enter the extracellular space. The resulting metabolic disorder is known as tumor lysis syndrome, a serious and sometimes life-threatening complication.Tumor lysis syndrome is the most prevalent oncological emergency. This syndrome is more commonly occurring in the treatment of highly proliferative tumors like Burkitt's lymphoma or acute leukemias, Patients with a leukocyte count >50.000 µl, LDH >5x higher than normal or hyperuricaemia >8 mg/dl are especially at risk. (80)

Tumor lysis can be differentiated into laboratory confirmed tumor lysis and clinically relevant tumor lysis. Cairo and Bishop defined the presence of laboratory tumor lysis if at least two of the following parameters raise about 25% during the first four days after the treatment: phosphate in serum, potassium, urea, uric acid; or calcium in serum decreases about 25%. Clinically relevant tumor lysis can be confirmed if one laboratory tumor lysis criterion is present and in addition one of the following: potassium >6mmol/l, creatinine >221 µmol/l, calcium <1.5 mmol/l, cardiac arrythmias, sudden cardiac death. (81)

Acute kidney failure, the risk of cardiac arrhythmias and epileptic seizures are the most concerning complications. Pathophysiologically, acute kidney failure within the tumor lysis syndrome involves various damage mechanisms. (39)

Urate Nephropathy: Precipitation of urate crystals in kidney tubules causes microvascular disorders, leading to a sudden decline in kidney function. Prophylactic measures, including xanthine oxidase inhibitors, have reduced the incidence of this type of damage.
Calcium Phosphate Precipitation: Increased calcium phosphate (>5 mmol2/l2), particularly in an alkaline environment, results in renal parenchymal calcifications, contributing to acute kidney failure. (39)

Xanthine/Hypoxanthine Crystal Formation: Therapy with xanthine oxidase inhibitors during severe tumor lysis syndrome can lead to renal damage caused by xanthine/hypoxanthine crystals. (39)

In treating tumor lysis syndrome, symptomatic therapy addresses accompanying laboratory chemical changes, including dialysis treatment. The approach involves intensified intravenous fluid administration and prophylactic use of xanthine oxidase inhibitors (such as allopurinol and febuxostat) in patients which are at risk of developing tumor lysis syndrome. In cases of severe hyperuricemia, rasburicase, which converts uric acid into the highly water-soluble product allantoin, may be considered. (82)

7. Dialysis in cancer patients

The renal function in HD patients is compromised, leading to potential issues with drug metabolism. This may necessitate adjustments to drug dosages to prevent overdosing and associated toxicity. Therefore, it's essential to carefully review drug prescriptions and available data of clinical studies, case reports and pharmacokinetics. Then appropriate dosage adjustments to ensure effectiveness while minimizing the risk of overdosing and side effects can be made. The clearance of drugs during dialysis needs to be considered when planning chemotherapy schedules as well. For most of cytotoxic drugs used in cancer treatment to patients undergoing dialysis no guidelines are established. Reducing the dosage of anticancer medications is often advised to prevent adverse reactions. However, if a drug is significantly removed by hemodialysis or not eliminated through the kidneys, reducing the dose may compromise its therapeutic effectiveness. Sometimes, dialysis needs to be precisely timed with chemotherapy administration to prevent toxicity. (83,84)

The extent to which a drug can be eliminated through extracorporeal renal replacement procedures depends on its molecular weight, protein binding, and distribution within the body. High molecular weight, significant protein binding, and extensive tissue distribution contribute to a lower extracorporeal elimination. Favorable conditions in all three factors facilitate effective elimination. Additional process-related factors, such as treatment duration, the type of dialysis membrane used, blood flow, and ultrafiltrate flow, also influence the elimination extent. Since these factors cannot be predicted with certainty, according to Czock and Sommerer, it is advisable to utilize pharmacokinetic studies whenever possible. In the absence of such studies, a rough estimate can be made based on criteria like a molecular weight <1000Da for low-flux membranes or <20,000Da for high-flux membranes, protein binding <80%, and an apparent volume of distribution <0.7 l/kg, indicating good elimination. (39,83)

In peritoneal dialysis, additional drug elimination is seldom relevant, as the extra drug clearance through peritoneal dialysis is usually ≤5 ml/min (equals ≤0.3 l/h), which is higher than the body's own drug clearance in anuria and negligible for many drugs (39).

7.1. Dosage adjustments and timing of cancer treatment

The objectives of adjusting drug dosages and scheduling cancer treatments for patients with impaired renal function aim to maintain treatment toxicity and efficacy within the levels observed in patients with normal kidney function. When medications are used regularly with short intervals, such as once a day, dosage adjustments can involve reducing the single dose, extending the dosing interval, or combining a reduced dose with an extended interval. For medications used cyclically every three weeks, adjustments may include reducing the single dose or lengthening the treatment cycle. In cases of cyclic, repeated use, adjustments might involve reducing the single dose, shortening the application phase, or extending the treatment cycle. Literature regarding the use of many antineoplastic agents in HD is either limited to a few case reports or small case series, or sometimes entirely lacking. There is more robust evidence available for the appropriate administration methods of drugs commonly used in clinical practice. The following Table contrasts the recommendations from two highly authoritative reviews on managing the most used drugs in HD patients. (39,83)

Therapy	Dosage proposed	Timing of dialysis
Carboplatin	AUC (area under the curve) +25	16-24h after HD. In case of high dose (200-300 mg/m2), HD after 1-2 hours.
Cisplatin	Reduction of 50%-75%	After HD
Fluorouracil/Capecitabin	Standard dose	Unclear if eliminated by HD. Not during HD.
Cyclophosphamide	Reduction 25%	After HD
Docetaxel	65mg/m2	Before or after HD
Doxorubicin	Standard dose	After HD
Epirubicin	Standard dose	After HD
Etoposide	Reduction of 40%–50%	Before or after HD
Gemcitabine	Standard dose	6–12 hours before HD
Ifosfamide	Not recommended	
Irinotecan	Reduced dose: 50 mg/m2/week	After HD
Methotrexate	Reduction of 75%, limited Data, not recommended	After HD
Oxaliplatin	Reduction of 30%	After HD
Paclitaxel	Standard dose	Before or after HD
Vinorelbine	Reduction of 25%–33%	After HD

Single agent chemotherapeutics dosage and timing proposal by Tomita et al., Janus et al. and Jäger et al.(39,84,85)

Literature describes a range of combination chemotherapy regimens and dialysis schedules, often excluding newer chemotherapeutic agents. While these publications have limitations, they serve as a foundation for identifying potential multiagent chemotherapy regimens suitable for dialysis patients. The following table outlines combination regimens that could be considered appropriate for patients with end-stage renal renal disease. (83)

Cancer type	Chemotherapy regimen	Dosage proposed	Timing of dialysis
Lung			
	CDDP+VNR	CDDP (25–50 mg/m2) day 1 + VNR (20 mg/m2/week) days 1, 8	1 hour after CT, daily
	CBDCA+VNR	CBDCA (AUC x 25) day 1 + VNR (20 mg/m2/week) days 1, 8	12–24 hours after CT
	CBDCA+DXL	CBDCA (AUC x 25), DXL (65 mg/m2) day 1	12–24 hours after CT
	CDDP+GEM	CDDP (25–50 mg/m2) day 1 + GEM (800 mg/m2) days 1, 8	1 hour after CDDP
	CDDP+TXL	CDDP (25–50 mg/m2) day 1 + TXL (175 mg/m2) day 1	1 hour after CDDP
	CBDCA+ETP	CBDCA (AUC 5×25) day 1 + ETP (50–100 mg/m2) days 1, 3	12–24 hours after HD
	CDDP+ETP	CDDP (25–50 mg/m2) day 1 + ETP (50–100 mg/m2) days 1, 3	1 hour after CDDP
		No available data supporting the use of pemetrexed	
GI cancer			
	FOLFOX6	OX (40–50 mg/m2), 5-FU and LV reduced by 70%–80%	1 hour after OXA infusion, 2 days later
	5-FU+LV	Standard dose	after CT
	CDDP+5-FU	CDDP (25–50 mg/m2) day 1, 5-FU (500 mg/m2 i.c.) day 1–5	1 hour after CDDP, every 2 days
	FOLFOXIRI	Standard dose reduced by 30%	1 hour after CPT-11 infusion, 2 days later
	+ bevacizumab	Standard dose	
	FOLFIRI	CPT-11 (180 mg/m2 and 125 mg/m2), 5-FU standard dose	1 hour after CPT-11
Breast cancer			
	Epirubicin+CTX	Epirubicin standard dose+CTX reduced of 25%	24 hours after CT
	Epirubicin+TXL	Standard dose	24 hours after CT
	FEC75	Epirubicin and 5-FU standard dose+CTX reduced of 25%	24 hours after CT

Germ cell tumours			
	CDDP+ETP	CDDP (14–20 mg/m2), ETP (50–100 mg/m2) days 1–4	Daily or on days 2 and 4
	CBDCA+ETP	CBDCA (100 mg/m2) day 1, ETP (50–100 mg/m2) days 1–4	On days 2 and 4
		On the basis of available data, the use of ifosfamide and bleomycin is not recommended	
Urothelial cancer			
	TXL+GEM	TXL (175 mg/m2) day 1+GEM (800 mg/m2) days 1, 8	24 hours after CT
	CBDCA+TXL	CBDCA (AUC 5×25) day 1 + TXL (175 mg/m2) days 1, 8	24 hours after CBDCA
	CBDCA+GEM	CBDCA (AUC 5×25) day 1 + GEM (800 mg/m2) days 1, 8	24 hours after CBDCA
	M-VAC	MTX (15 mg/m2), CDDP (40 mg/m2), VLB (1.8 mg/m2), DX (18 mg/m2) day 1	1 hour after CDDP
	VAC	CBDCA (100 mg/m2), VLB (3 mg/m2), DX (22.5 mg/m2) day 1	24 hours after CBDCA

(CDDP, cisplatin; VNR, vinorelbine; DXL, docetaxel; TXL, taxol; ETP, etoposide; FOLFOX6, fluorouracil (FU), oxaliplatin (OXA), leucovorin (LV); FOLFOXIRI: FU, OXA, irinotecan, LV; FEC, FU, epirubicin, cyclophosphamide; GEM, gemcitabine; CT, chemotherapy; i.c., continuous infusion; M-VAC, methotrexate, vinblastine, doxorubicin, CDDP)

Multi agent chemotherapy regimens dosage and timing proposal by Pedrazolli et al. and Jäger et al. (39,83)

8. Ethical considerations

Dialysis serves as a life-sustaining organ replacement therapy that prolongs life. In cases of end-stage renal failure, discontinuing dialysis typically leads to death within 10 days, but can extend to 3 weeks, depending on residual kidney function. (86)

While the exact frequency of dialysis discontinuation as a cause of death in Germany remains unquantified, data of other high-income countries like the US, Australia, New Zealand, UK and the Netherlands are available. Up to 30% of adult dialysis patients were intentionally

ending dialysis and died from withdrawal. Factors affecting discontinuing of dialysis are older age, multiple comorbidities, dementia, severe pain, residing in care facilities, and relying more on external assistance. Factors like, Caucasian ethnicity, female gender, and higher education also influence discontinuation rates. (87–90)

Besides these general factors, concrete reasons to withdraw HD are multiple failures in hemodialysis access, sudden medical issues like frequent low blood pressure, intense pain, muscle spasms, or life-threatening heart rhythms, persistent health challenges, long-term decline in health and frailty, logistical and financial barriers, like extended travel distances, membership in impoverished rural or tribal communities and insufficient family support. (91,92)

The American Society of Nephrology (ASN) and the Renal Physicians Association (RPA) released joint guidelines in 2000, considering ethical principles, evidence-based medicine, and US legal context. These guidelines advocate for "shared decision making" a nine-step process for initiating or discontinuing dialysis. Such decisions should be discussed with patients facing limited life expectancy, reduced quality of life, untreatable pain, or progressive disease decline. Decisions to discontinue dialysis may originate from patients, nephrologists, general practitioners, nursing staff, or relatives. The process involves collaborative decision-making with healthcare providers, patients, and often involves family members, team members, psychologists, and ethicists. Patients should understand their prognosis. If incapable of consenting, legal representatives act on their behalf. Involvement of doctors in decision-making can alleviate relatives' guilt. The guidelines also emphasize the need for continued palliative care and offer insights into the psychosocial and spiritual aspects of end-of-life care. (93)

9. Conclusions and Suggestions

9.1. Conclusion

Cancer is characterized by abnormal cell growth due to alterations in gene expression, disrupting the balance between cell proliferation and death. Malignant tumors can invade surrounding tissues, spread to lymph nodes, and metastasize to distant organs. In 2020, there were an estimated 19.3 million new cancer cases and 10.0 million cancer-related deaths worldwide. Female breast cancer was the most diagnosed cancer globally, followed by lung cancer. Lung cancer accounted for the highest number of cancer deaths globally, followed by

liver and stomach cancers. In Germany, approximately 500,000 new cancer cases were reported in 2020.

Kidney failure can be acute or chronic, with chronic kidney disease being a continuously worsening condition. CKD is prevalent worldwide, with a global CKD prevalence of 13.4% and stages 3-5 CKD at 10.6%. In Germany, approximately 2.3% of people aged 18-79 years have an eGFR <60. Dialysis is the primary treatment for end-stage renal disease, with hemodialysis being the most common method.

Dialysis aims to remove waste products, correct electrolyte imbalances, and maintain fluid balance. Acute and chronic indications for dialysis include anuria, elevated serum creatinine, hyperuricemia, hyperkalemia, metabolic acidosis, and symptoms of uremia. Hemodialysis and peritoneal dialysis are the two main types of dialysis. Hemodialysis uses a machine to filter blood, while peritoneal dialysis uses the patient's peritoneum as a filter. Hemofiltration and hemodiafiltration are variations of hemodialysis that offer different advantages and are primarily used in acute kidney injury cases.

Cancer and kidney disease often coexist and can complicate each other's management. Kidney complications in cancer patients can arise from the tumor itself, chemotherapy, immune checkpoint inhibitors, tyrosine kinase inhibitors, and surgery. Acute kidney injury is a prevalent complication in cancer treatment, affecting treatment outcomes and patient survival. CKD can develop as a result of pre-existing renal insufficiency, the malignant disease itself, or therapy-related factors.
The kidney's susceptibility to damage stems from its high blood flow rate (25% of cardiac output), exposing it to foreign substances in the blood. The kidney's concentration processes can lead to toxic substance levels due to its reabsorption mechanisms.

Both conventional and modern cancer treatments can be nephrotoxic. Standard cancer treatments, like cisplatin, methotrexate, ifosfamide, and gemcitabine can cause direct damage to proximal tubules, induce renal damage through crystal nephropathy or cause thrombotic microangiopathy. Newer therapies like immune checkpoint inhibitors, can lead to renal side effects by disrupting immune system self-tolerance. Acute interstitial nephritis is the most common kidney complication. Renal complications, especially acute kidney injury, can occur in up to 29% of patients, particularly when using combination therapies.

Renal function in hemodialysis patients is compromised, affecting drug metabolism. Dosage adjustments are crucial to prevent drug toxicity while maintaining therapeutic efficacy. The choice and timing of chemotherapy should consider the patient's dialysis schedule.

Decisions about discontinuing dialysis can arise due to various factors, including age, comorbidities, and financial barriers. Shared decision-making involving healthcare providers, patients, and family members is crucial in such cases, emphasizing the importance of understanding the patient's prognosis and providing palliative care.

In conclusion, kidney complications in cancer patients can arise from the disease itself or its treatments. Understanding the mechanisms and risk factors can help in early detection, prevention, and management of renal complications in these patients.

9.2. Suggestion for further research

Further studies are needed to identify optimal chemotherapy regimens that are effective against cancer, while minimizing renal toxicity in patients with kidney impairment. There is still a lack of pharmacokinetic data on the interaction between dialysis and chemotherapeutic drugs, since most of the existing data consist of case reports and small case series.

9.3.Recommendations for improving dialysis outcomes in cancer patients

To improve dialysis outcomes in cancer patients, it is crucial to focus on early detection and monitoring of kidney function, tailor chemotherapy regimens based on renal status, and promote collaborative care between oncologists and nephrologists as well as considering pharmacokinetic studies for personalized dosing. Educate patients on adherence, fluid management, and symptom reporting, while providing supportive care for nephroprotective strategies.

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