

Chapter 2: Why Do We Need an Onco-Nephrology Curriculum?

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As health care providers, we are acutely aware of the National Vital Statistics Report describing the significant toll cancer, as the second leading cause of death, has on our patients (1). Importantly, cancer incidence rates are highest in the elderly (2). At the same time, the US Renal Data System (USRDS) notes that AKI rates are increasing in the elderly, with rates 10-fold higher than the nonelderly population (3). Importantly, both AKI and CKD are highly prevalent in cancer patients, in particular renal cell cancer, liver cancer, multiple myeloma, leukemias, and lymphomas (4,5). The Belgian Renal Insufficiency and Anticancer Medication (BIRMA) study noted the frequent occurrence of kidney disease in five major cancers (Figure 1) (6). Most concerning is the increased mortality noted in patients with AKI/CKD compared with those without kidney disease. For instance, the development of AKI can be associated with cessation of effective chemotherapeutic regimens, or the presence of preexisting CKD may limit the use of otherwise active regimens that may be curative. This combination of cancer, kidney disease, and mortality has led to the recognition that nephrology and oncology are intricately linked and require our full attention as a subspecialty (Figure 2). Hence, “onco-nephrology” was born in a few large centers but has steadily grown to include many medical centers, hospitals, and clinics.

What exactly is onco-nephrology? It is a rapidly growing area of nephrology where kidney disease in cancer patients has become an important source of consultations, with the trend occurring over the last 10–15 years. Oncology patients now make up a significant number of the patients that nephrologists see for kidney-related problems in the outpatient clinic, on the inpatient floors, and in the medical intensive care unit (ICU). There is an increase in the number of patients with kidney disease, in part related to high incidence rates for many malignancies, as well as improvement in the cancer death rates due to more

effective chemotherapeutic agents, including biologics, and stem cell therapies. However, this has led to an increase in the number of cancer survivors that often develop acute and/or CKD due to their malignancy and/or its associated treatment. The best example of the bidirectionality of cancer and kidney disease is seen between renal cancer and CKD (Figure 3).

Cancer can directly injure the kidneys through tumor infiltration or production of nephrotoxic (paraneoplastic) substances. Any one of the growing numbers of therapeutic agents that extend patient lives can cause various types of acute or CKD, along with serious electrolyte and acid–base abnormalities. In addition, patients may develop multiorgan illness requiring ICU-level care and RRT. Certain malignancies are more likely to cause this severe form of multiorgan dysfunction and may be associated with higher mortality rates. When this type of critical illness occurs in the setting of advanced malignancy, it raises questions about the appropriateness of aggressive care in “futile situations” and the role of palliation. Thus, care for oncology patients has become more specialized and complicated, requiring collaboration between nephrologists, oncologists, intensivists, and palliative care specialists.

The remarkable advances in cancer management present both new opportunities and complex challenges for the oncology and nephrology communities. It is essential for nephrologists to be informed and actively involved in certain facets of cancer care. A better understanding of the rapidly evolving field of cancer biology and its therapy is required for nephrologists to become valuable members of the

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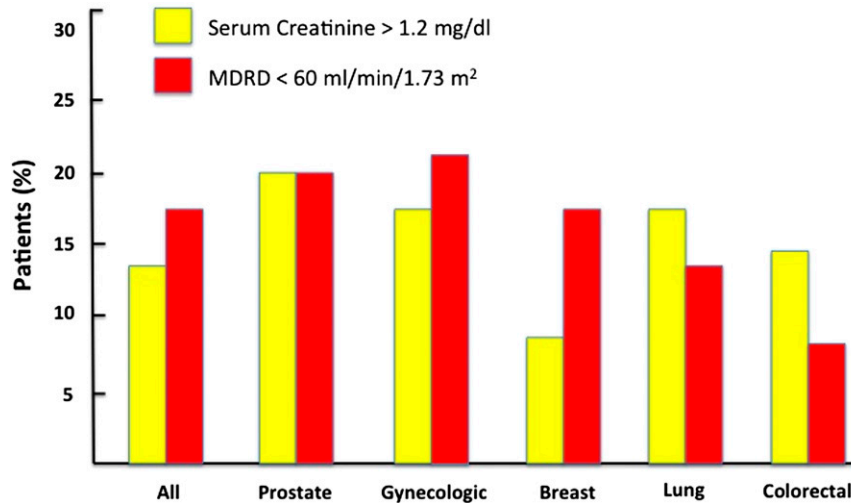


Figure 1. Kidney injury associated with five different cancers in the BIRMA study. The percentage of patients with kidney injury as defined by SCR, GFR <90, or GFR <60 is noted both for the individual cancers and all cancers lumped together. BIRMA, Belgian Renal Insufficiency and Anticancer Medication study; SCR, serum creatinine; aMDRD, abbreviated MDRD. Adapted with permission from reference 6.

cancer care team and to provide the best nephrology care possible. The goal of this American Society of Nephrology (ASN) sponsored Onco-Nephrology core curriculum is to provide the ASN membership including veteran nephrologists, newly minted nephro-clinicians, and fellowship trainees with the building blocks on which further information can be added as technology advances. This educational venue will be available outside the ASN membership as well.

Nephrologists must be well prepared to care for patients with cancer and its associated renal complications. The renal manifestations of cancer have many unique features, and these conditions often require specialized approaches to manage fluid, electrolyte, and acid–base disturbances, as well as acute

and chronic kidney injury. Furthermore, the ever-evolving field of cancer therapy demands a comprehensive team approach with the nephrologist as one of the critically important care providers. As such, it is essential for nephrologists to develop expertise in the practice of onco-nephrology. We hope this curriculum provides the initial framework to achieve this goal.

TAKE HOME POINTS

- Kidney disease is a frequent and increasing complication of cancer.
- There is a bidirectional relationship between cancer and kidney disease.

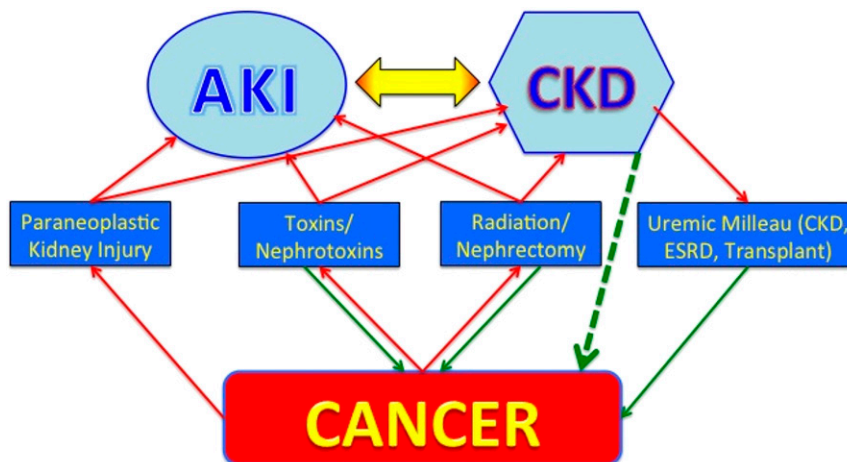


Figure 2. The relationship between cancer and AKI and CKD. Cancer, AKI, and CKD are linked by various exposures and pathways.

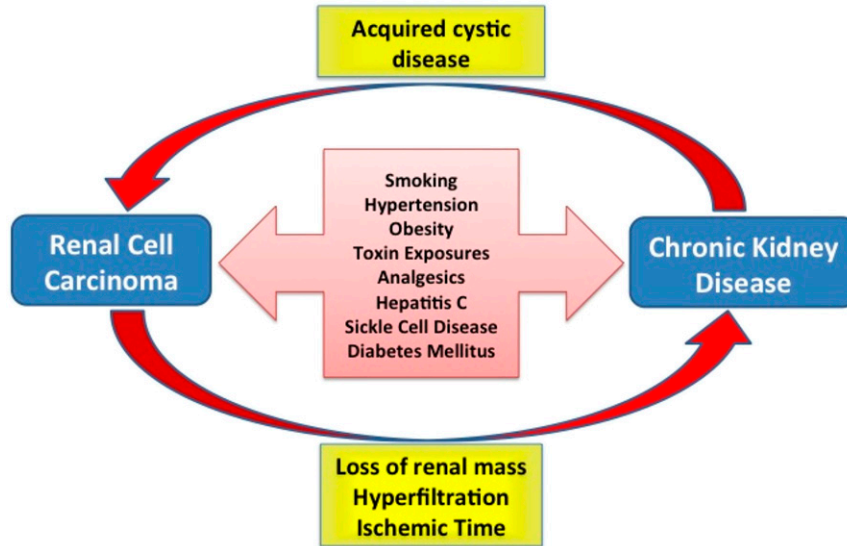


Figure 3. The bidirectionality between renal cancer and CKD. Common exposures that can cause both renal cell cancer and CKD are noted in the middle bidirectional arrow.

- Onco-nephrology is a growing area of nephrology that requires clinicians to have a better understanding of the renal complications of cancer including electrolyte/acid–base disturbances, AKI, and CKD.
- The Onco-Nephrology Curriculum is an educational tool created by ASN Onco-Nephrology Forum members and other expert nephrologists.

REFERENCES

1. Hoybert DL, Xu J. Deaths: Preliminary data for 2011. *Natl Vital Stat Rep* 61: 2012
2. National Cancer Institute. Age-adjusted SEER incidence rates, 2007–2011 (Table 2.7). SEER cancer statistics review (CSR) 1975–2011. Surveillance, epidemiology, and end results program. Available at: http://seer.cancer.gov/csr/1975_2011/browse_csr.php?sectionSEL=2&pageSEL=sect_02_table.07.html. Accessed March 1, 2015
3. USRDS. Percent of Medicare patients aged 66+ (a) with at least one AKI hospitalization, and (b) with an AKI hospitalization that had dialysis by year, 2003–2012 (Figure 5.1). Chapter 5: Acute kidney injury. Available at: http://www.usrds.org/2014/view/v1_05.aspx. Accessed March 1, 2015
4. Christiansen CF, Johansen MB, Langeberg WJ, Fryzek JP, Sørensen HT. Incidence of acute kidney injury in cancer patients: A Danish population-based cohort study. *Eur J Intern Med* 22: 399–406, 2011
5. Schmid M, Abd-El-Barr AE, Gandaglia G, Sood A, Olugbade K Jr, Ruhotina N, Sammon JD, Varda B, Chang SL, Kibel AS, Chun FK, Menon M, Fisch M, Trinh QD. Predictors of 30-day acute kidney injury following radical and partial nephrectomy for renal cell carcinoma. *Urol Cancer* 32: 1285–1291, 2014
6. Janus N, Launay-Vacher V, Byloos E, Machiels JP, Duck L, Kerger J, Wynendaele W, Canon JL, Lybaert W, Nortier J, Deray G, Wildiers H. Cancer and renal insufficiency results of the BIRMA study. *Br J Cancer* 103: 1815–1821, 2010

REVIEW QUESTIONS

1. Which of the following malignancies has the highest 1-year risk for AKI?
 - a. Multiple myeloma
 - b. Lymphoma
 - c. Renal cell cancer
 - d. Liver cancer
 - e. Leukemia

Answer: c is correct. Although all of these cancers are associated with increased AKI risk, renal cell cancer was found to have the highest 1-year risk in a cohort study examining the incidence of AKI in cancer patients (4).

2. In a patient with a recent diagnosis of cancer, which of the following complications are increased in the setting of the cancer diagnosis?
 - a. AKI
 - b. CKD
 - c. Mortality
 - d. All of the above

Answer: d is correct. Cancer is associated with an increased incidence of AKI, CKD, and overall mortality. These complications are the result of the tumor itself (infiltration or tumor products), drug nephrotoxicity, comorbid diseases, or all of the above.