

# Chapter 19: Palliative Care in Patients with Kidney Disease and Cancer

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## INTRODUCTION

Many, if not most, cancer and kidney disease patients have two things in common: they have a shortened life expectancy and a high symptom burden. Both populations benefit from early palliative care interventions. The goal of palliative care is to relieve suffering and to support the best possible quality of life for patients and their families, regardless of their stage of disease or the need for other therapies, in accordance with their values and preferences. By Medicare regulation, hospice care is limited to patients estimated to be in their last 6 months of life if their disease follows the normal course. In patients with kidney disease and cancer (hereafter kidney-cancer patients) who have a higher symptom burden than patients with either disease alone, the need for meticulous pain and symptom management is even more important to maintain quality of life. In addition, there is a unique need for advance care planning for these patients, most of whom have two life-limiting illnesses. As in other populations, for kidney-cancer patients, pain is one of the most common and severe symptoms. Multiple studies in kidney patients show that pain is undertreated. Treatment of pain in patients with stage 4 and 5 CKD and ESRD is more challenging because of the failure of renal excretion of active metabolites from some commonly used opioids, which leads to opioid neurotoxicity. The nephrology community has developed a clinical practice guideline that endorses the process of shared decision-making in reaching decisions about who should undergo dialysis. It recognizes that the burdens of dialysis may substantially outweigh the benefits in some patients and notes that nephrologists may want to recommend forgoing dialysis to kidney-cancer patients who are terminally ill from their cancer.

This chapter describes the growing interest in the nephrology and oncology communities in incorporating palliative care into the standard treatment of patients with CKD, ESRD, and cancer.

## RELEVANCE OF PALLIATIVE CARE

There is an increasing recognition that skills in palliative and end-of-life care are required for physicians, nurses, and others who treat patients who have CKD and ESRD (Table 1). The principal reasons are as follows: first, they have a significantly shortened life expectancy; just over half of dialysis patients (52%) are still alive 3 years after the start of RRT (1).

Second, patients with CKD and ESRD have multiple comorbidities and consequently many symptoms such as pain, fatigue, itching, and difficulty with sleep. In one study, the symptoms of CKD and ESRD patients were found to be comparable (mean of 10.7) and severity (2). Similarly, cancer patients have been found to have a high symptom burden compared with age-matched controls, and pain, anxiety and depression, and insomnia were noted as most prevalent in a population-based study of 1,904 cancer survivors (3). An interaction between cancer status and comorbidity was found, resulting in a higher symptom burden for patients with comorbidities such as CKD. Thus, it is reasonable to conclude the CKD or ESRD patients with cancer will have a higher symptom burden than patients with either cancer or kidney disease alone (3).

Third, the dialysis population has been growing progressively older. The incidence rates of ESRD are highest in patients 75 years old and older, and they continue to rise in this group (1). Older patients survive the shortest period of time on dialysis, and they withdraw from dialysis significantly more often than younger patients.

In consideration of the high symptom burden and the low survival rate for dialysis patients, the

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**Table 1. Palliative care for CKD/ESRD patients: Need for a systematic approach**

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Pain and symptom assessment/management (11,21)  
Shared decision-making for informed consent  
Patient-specific estimates of prognosis using the surprise question  
Timely discussions prompted by prognosis  
Inclusion of family/legal agent in discussions  
Completion of advance directives  
Completion of physician orders for life-sustaining treatment (POLST) paradigm form as appropriate  
Immediately actionable medical orders  
Transferrable throughout health care setting  
Referral to hospice when indicated

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Adapted from reference 5.

American Society of Nephrology (ASN) and the Renal Physicians Association (RPA) have recommended that dialysis facilities incorporate palliative care into their treatment of patients (4,5). Nephrologists have been encouraged to obtain education and skills in palliative care, and dialysis facilities have been urged to develop protocols, policies, and programs to ensure that palliative care is provided to their patients (Table 2) (5). Also, dialysis units have been urged to develop a working relationship with local hospice programs, so patients with ESRD who stop dialysis or patients undergoing dialysis with a nonrenal terminal diagnosis may be referred for hospice. Similarly, the American Society of Clinical Oncology has issued a provisional clinical opinion that early involvement of palliative care when combined with standard cancer care leads to better patient and caregiver outcomes, including improvement in symptoms, quality of life, and patient satisfaction and reduced caregiver burden (6).

## SYMPTOM MANAGEMENT

### Pain

As in other patient populations, the burden of symptoms for patients undergoing dialysis is inversely associated with their reported quality of life (7). Pain is one of the most common symptoms reported by patients undergoing dialysis, and several studies have found that approximately 50% of these patients report pain. For most patients undergoing dialysis, the pain is musculoskeletal in origin. Smaller numbers of patients have pain related to the dialysis procedure, peripheral neuropathy, peripheral vascular disease, or carpal tunnel syndrome. Three studies have found that pain is undertreated in 75% of patients undergoing dialysis (8–10). As in cancer patients, use of the World Health Organization (WHO) three-step analgesic ladder has been found to be effective in the treatment of pain in dialysis patients (9). Because the metabolites of some of the opioids on the analgesic ladder are renally excreted and active, these opioids, morphine, codeine, meperidine, and propoxyphene, are not recommended for use in patients with advanced kidney disease (Table 3) (11).

**Table 2. Components of a dialysis facility palliative care program**

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1. Palliative care focus
  - a. Educational activities, including dialysis unit in-service trainings
  - b. Quality improvement activities, including morbidity and mortality conferences
  - c. Use of the “Would you be surprised if this patient died within the next year?” question to identify patients appropriate for palliative care
  - d. Collaboration with local hospice programs to coordinate a smooth transition to end-of-life care
2. Pain and symptom assessment and management protocols
3. Systematized advanced care planning
4. Psychosocial and spiritual support to patients and families, including the use of peer counselors
5. Terminal care protocols that include hospice referral
6. Bereavement programs for families that include memorial services

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Adapted from reference 5.

Morphine is the best studied of the opioids used for pain management, and its most common metabolites (including morphine-3-glucuronide, morphine-6-glucuronide, and normorphine) are excreted by the kidneys. The clearance of these metabolites is particularly problematic in stage 4 and 5 CKD and ESRD. Morphine-6-glucuronide is an active metabolite with analgesic properties; it crosses the blood–brain barrier and may have prolonged central nervous system effects. A comprehensive review recommended that morphine not be used in patients with kidney disease because it is so difficult to manage the complicated adverse effects of the morphine metabolites (12).

Studies of codeine pharmacokinetics suggest that codeine metabolites would accumulate to toxic levels in a majority of patients undergoing hemodialysis. Codeine use is not recommended because serious adverse effects have been reported in patients with CKD (12).

Hydromorphone is metabolized in the liver largely to hydromorphone-3-glucuronide. This metabolite accumulates in patients with kidney disease and can cause opioid neurotoxicity. Some studies suggest that hydromorphone is removed with dialysis. It is recommended that hydromorphone be used cautiously, if at all, in patients stopping dialysis (12).

Use of oxycodone in patients with kidney disease has not been well studied. The elimination half-life of oxycodone is

**Table 3. Pain medications for use in advanced kidney failure**

Recommended	Use with caution	Do not use
Fentanyl	Tramadol	Morphine
Methadone	Hydrocodone/oxycodone	Codeine
Hydromorphone	Desipramine/nortriptyline	Meperidine
Acetaminophen		Propoxyphene
Gabapentin		

Adapted from reference 11. See <http://www.kidneysupportivecare.org/Files/PainBrochure9-09.aspx> for recommendations for use, dosage reductions, and cautions in advanced kidney failure.

lengthened in dialysis patients, and excretion of metabolites is impaired but almost all are inactive. Oxycodone can be used with caution in patients with advanced CKD and ESRD (12).

The WHO analgesic ladder recommends the use of fentanyl for severe pain. Fentanyl is metabolized in the liver primarily to norfentanyl. There is no evidence that any fentanyl metabolites are active. Several studies have found that fentanyl can be used safely in patients with CKD and ESRD. It has negligible dialyzability. Fentanyl use is deemed to be one of the safest opioids to use in patients with advanced CKD (12).

The WHO analgesic ladder recommends methadone for severe pain. Studies in anuric patients have found that nearly all of methadone and its metabolites doses are excreted in the feces. No dose adjustments are recommended for patients undergoing dialysis. The use of methadone appears safe in patients with advanced CKD and ESRD (12).

Opioids are also often used to treat dyspnea at the end of life in patients with CKD, ESRD, and cancer. In the setting of worsening renal function or withdrawal of dialysis, the clinician may be challenged to distinguish uremic encephalopathy from opioid neurotoxicity. Both can cause sedation, hallucinations, and myoclonus. If respiratory depression is also present, it is advisable to stop the opioid until the respiratory depression subsides. If the patient's respiratory rate is not compromised, the opioid can usually be continued, and a benzodiazepine such as lorazepam is added to control the myoclonus. Occasionally, a lorazepam continuous intravenous infusion at 1 or 2 mg/h is necessary to control the myoclonus.

Although nonsteroidal anti-inflammatory drugs are recommended for use in step 1 on the WHO analgesic ladder, the use of these drugs in patients with CKD is contraindicated because of their nephrotoxicity and in dialysis patients because of the increased risk of upper gastrointestinal bleeding.

The Mid-Atlantic Renal Coalition and the Coalition for Supportive Care of Kidney Patients assembled a panel of international experts on pain management in CKD and developed an evidence-based algorithm for treating pain in dialysis patients that is accessible online (11).

### **Other symptom management**

Because of their comorbid illnesses, patients undergoing dialysis are among the most symptomatic of any population with chronic disease. In one study (13) of 162 patients undergoing dialysis from three different dialysis units, the median number of symptoms reported by patients was 9.0. Pain, dyspnea, dry skin, and fatigue were each reported by >50% of the patients. Of the 30 different symptoms reported by the patients, the 6 most bothersome (starting with the most severe first) were as follows: chest pain, bone or joint pain, difficulty becoming sexually aroused, trouble falling asleep, muscle cramps, and itching.

Pruritus, or itching, is one of the most frustrating symptoms experienced by CKD and ESRD patients. Secondary hyperparathyroidism, increased calcium-phosphate deposition in the skin, dry skin, inadequate dialysis, anemia, iron deficiency, chronic inflammation, imbalance in endogenous opioids,

neuropathic processes, and low-grade hypersensitivity to products used in the dialysis procedure have all been identified as possible contributory factors. In addition to careful management of all these factors, the following interventions have been tried for pruritus with some success: emollient skin creams, phototherapy with ultraviolet B light three times weekly, intravenous lidocaine during dialysis for refractory itching, gabapentin, naltrexone, and thalidomide (14).

### **ADVANCE CARE PLANNING**

Advance care planning is a process of communication among patients, families, health care providers, and other important individuals about the patient's preferred decision-maker and appropriate future medical care if and when a patient is unable to make his or her own decisions. Advance care planning has been recommended as a central tenet of CKD, ESRD, and cancer patient care (15). It is especially appropriate because of the life-limiting nature of these diseases. The "surprise" question—would I be surprised if this patient died in the next year?—has been validated in both the ESRD and cancer patient populations as a reliable trigger to identify patients who are at increased risk of death within 1 year and for whom palliative care consultation including advance care planning is appropriate (16,17).

Researchers have developed an evidence-based robust integrated prognostic model with a C-statistic of 0.8 to estimate dialysis patients' 6- and 12-month survival (18), which is available online at [www.touchcalc.com/calculators/sq](http://www.touchcalc.com/calculators/sq). The American Society of Nephrology and Renal Physicians Association have recommended that advance care planning for CKD and ESRD patients including a patient-specific estimate of prognosis and shared decision-making occur prior to the initiation of dialysis (5,19). Nephrologists are responsible for advance care planning, although aspects of it can be delegated to other nephrology personnel (15). Advance care planning is important for kidney-cancer patients because it can ensure that patients' wishes for end-of-life care are respected, that unwanted interventions are avoided, and that patients and their families are satisfied with the care provided (15). Although nephrologists are expected to possess primary palliative care skills, they are encouraged to consult palliative care physicians for more complex cases (20). Table 2 presents a comprehensive approach to incorporating palliative care into dialysis facility patient care.

### **CONCLUSIONS**

There is a growing commitment among the leadership in the nephrology and oncology communities to enhance palliative care for advanced kidney disease and cancer patients. It is highly likely that palliative care for these patients will be significantly improved over the next decade, as nephrologists, oncologists, and palliative care consultants apply the knowledge and skills discussed in this chapter.

## TAKE HOME POINTS

- Early palliative care intervention is becoming the standard of care for kidney-cancer patients. It improves patients' quality of life and respects their treatment wishes.
- CKD, ESRD, and cancer patients have shortened life expectancy. The 5-year survival rate for incident dialysis patients is 40%, which is 30% less than that of incident cancer patients (66%).
- Because they do not have active metabolites excreted by the kidneys, fentanyl and methadone are the safest drugs to use for severe nociceptive pain in patients with advanced kidney disease.
- Palliative care consultation can help with complex pain and symptom management and advance care planning, including shared decision-making about the goals of care. Collaboration with hospices can help dialysis units implement a palliative care program and appropriately refer patients for hospice care at the end of life.

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## REVIEW QUESTIONS

1. Which one of the following is an advantage of the physician orders for life-sustaining treatment (POLST) form compared with an advance directive for a patient with stage 5 kidney disease, terminal cancer, and loss of decision-making capacity?
  - a. It is legal in all fifty states
  - b. It is an immediately actionable medical order
  - c. Checklist format prevents contradictory orders from being issued
  - d. It is appropriate for patients in all stages of CKD

Answer: b is correct. The POLST form or variant is endorsed in 22 states at present and being developed in another 23. Contradictory orders could be written between Sections A and B such that the patient is to receive CPR in Section A and comfort measures in Section B of the form. The form is only appropriate for patients who are seriously ill and for whom the physician would not be surprised if the patient died in the next year.

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2. Which one of the following medications would be the preferred, recommended medication for a patient with stage 5 CKD and lung cancer with painful metastases to the bone who describes his pain as aching and 10/10?
  - a. Morphine
  - b. Acetaminophen
  - c. Codeine
  - d. Fentanyl

Answer: d is correct. Fentanyl is appropriate for severe nociceptive pain in patients with advanced kidney failure.

Fentanyl does not have active metabolites excreted by the kidneys. Morphine and codeine are contraindicated in advanced kidney failure because of the toxic accumulation of active metabolites in kidney failure. Acetaminophen is not appropriate for severe pain.

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3. Which one of the following statements best summarizes the role of shared decision-making for patients with advanced kidney disease and cancer approaching the need for dialysis?
  - a. Shared decision-making is an outmoded concept from the 1980s
  - b. Shared decision-making fits well with a disease-oriented approach to CKD patient treatment
  - c. Shared decision-making for CKD patients defaults to dialysis modality choices
  - d. Shared decision-making is the recognized preferred model for medical decision-making

Answer: d is correct. Shared decision-making was introduced in the 1980s as a process to promote informed consent and decisions that adequately take account of patients' preferences. It fits well with an individualized, patient-centered approach to decision-making and not a disease-oriented approach. Shared decision-making for CKD patients encompasses decisions about whether to start or stop dialysis and not just dialysis modality.

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