The Ethics of End-of-Life Care for Patients with ESRD

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Summary
Patients with ESRD have extensive and unique palliative care needs, often for years before death. The vast majority of patients, however, dies in acute care facilities without accessing palliative care services. High mortality rates along with a substantial burden of physical, psychosocial, and spiritual symptoms and an increasing prevalence of decisions to withhold and stop dialysis all highlight the importance of integrating palliative care into the comprehensive management of ESRD patients. The focus of renal care would then extend to controlling symptoms, communicating prognosis, establishing goals of care, and determining end-of-life care preferences. Regrettfully, training in palliative care for nephrology trainees is inadequate. This article will provide a conceptual framework for renal palliative care and describe opportunities for enhancing palliative care for ESRD patients, including improved chronic pain management and advance care planning and a new model for delivering high-quality palliative care that includes appropriate consultation with specialist palliative care.

Approximately 90,000 dialysis patients die each year in the United States, with a high annual unadjusted mortality rate of approximately 20% (1). The exact numbers of patients with ESRD who die without starting dialysis are unknown but estimated to be several fold higher. As of December 31, 2009, there were 397,796 people in the United States on dialysis (1). The prevalent population ages 75 years and older is the largest growing group, having nearly doubled since 1997 (1).

Patients with ESRD experience an extremely high burden of symptoms similar to those symptoms of cancer patients hospitalized in palliative care settings (2–8), and they have extensive and unique palliative care needs, often for years before death (9,10). Dialysis patients are more frequently dying after withdrawal of dialysis (10–15% in 1990 and 20% in 2004) (1), representing the second leading cause of death after cardiovascular disease. Unfortunately, most patients lack decision-making capacity at the time that the decision to withdraw dialysis is made and are not involved in these decisions (11). Most dialysis patients do not have an advance directive and have not had discussions with their family or health providers about their end-of-life care preferences (10), despite patients wanting to engage in these conversations (10,12). Even patients with advance directives often do not address health states in which they would no longer wish to continue dialysis (13,14). Only a minority of patients chooses to forgo cardiopulmonary resuscitation (10,15), because they are unaware of the poor likelihood of survival after cardiopulmonary resuscitation (16). Without advance care planning (ACP), neither family nor physicians is accurate in their predictions of patients’ desires about life-sustaining treatments, including wishes for ongoing dialysis (17).

Although palliative care is recognized as a basic human right (18), the vast majority of ESRD patients die in acute care facilities without accessing palliative care services (19), despite indicating preferences for home death (10). Dialysis patients ≥65 years old have very high rates of hospitalization, intensive care unit admission, and intensive procedures in the final month of life, with care being more aggressive than the care reported for cancer and heart failure patients (20). Poor-quality hospitalized deaths began to improve for patients dying with cancer as a result of an increasing emphasis on providing palliative care. Similar systematic attention has not yet been paid to patients dying with ESRD. This article will provide a conceptual framework for renal palliative care and describe opportunities for enhancing palliative care for ESRD patients, including improved chronic pain management and ACP and a new model for delivering high-quality palliative care that includes appropriate consultation with specialist palliative care.

A Conceptual Framework for Renal Palliative Care

What Is Palliative Care?
There have been several transitions in terminology relating to care near the end of life from hospice and terminal care in the early phases of the hospice movement in the United Kingdom and end-of-life...
care, which is now widely used in North America, to palliative care. More recently, supportive care has emerged as a popular term to describe noncurative treatments for both cancer and noncancer patients (21). As a result, there is tremendous confusion about what constitutes palliative care. This review focuses on palliative care as defined by the World Health Organization. “Palliative care is an approach that improves the quality of life of patients and their families facing the problem associated with life-threatening illness, through the prevention and relief of suffering by means of early identification and impeccable assessment and treatment of pain and other problems, physical, psychosocial and spiritual” (22). This process of care affirms life and regards dying as a normal process; it intends to neither hasten nor postpone death. It offers a support system to help patients live as actively as possible until death, it enhances quality of life, and it may also positively influence the course of illness. Palliative care principles should be applied on diagnosis of ESRD (Figure 1). Physical, psychosocial, and spiritual symptom management would come into the care plan, as needed, in support of other therapies, such as chronic dialysis, that are intended to prolong life. In this way, palliative care becomes a gradual and normal transition within the care process.

Clinical Practice Guidelines for Renal Palliative Care

There is growing international interest in a comprehensive analysis of the evidence around renal palliative care to develop global guidelines for implementation of renal palliative care. This analysis would help improve worldwide practice, referral, and overall access to palliative care services for patients with ESRD. At this time, however, there are no formal standards to inform how to best deliver and assess renal palliative care. As a preliminary step, the Renal Physicians Association recently updated the clinical practice guideline, *Shared Decision Making in the Appropriate Initiation of and Withdrawal from Dialysis*, to assist nephrologists, patients, and families in reaching decisions on whether to initiate or stop dialysis (23). Nephrologists who are knowledgeable of this guideline report greater preparedness to make end-of-life decisions (24). The American Society of Nephrology recently identified shared decision-making between patients, their families, and their physicians when initiating chronic dialysis as one of the top five priorities for ensuring quality patient care. These guidelines include recommendations for the provision of renal palliative care, including elicitation of patient goals and preferences, and discussion of prognosis and expected benefits and harms of dialysis within the context of patients’ goals and preferences (25). The United Kingdom has implemented a national strategy for renal palliative care that focuses on timely ACP and appropriate linking of renal care with the primary care community and palliative care services (26). However, considerable variation in the provision of palliative care remains, and most nephrologists still feel insufficiently prepared to deal with the numerous end-of-life challenges inherent in the care of their patients (24,27). With the increasing awareness of the need for a more systematic approach to renal palliative care, a framework (Figure 2) is emerging, predominantly in Canada and the United Kingdom, to guide and support health professionals, patients, and families throughout patients’ illness with ESRD (28).

Identifying ESRD Patients Most Likely to Benefit from Palliative Care Services

ESRD patients at highest risk of early death or patients with the most suffering, whether physical, psychosocial, or spiritual, are likely to obtain the greatest benefit from palliative care services. A successful renal palliative care program will depend, in part, on the ability to successfully identify these patients. The following discussion includes two areas in which palliative care services would be indicated, chronic pain management and ACP, and it will address strategies to help identify patients in need of these services.

Improving Palliative Care for ESRD Patients

Chronic Pain Management in ESRD

Chronic pain is experienced by approximately 50% of ESRD patients, with 82% of patients reporting this pain as moderate or severe in intensity (29). Pain has devastating effects on ESRD patients’ quality of life (5,30,31), with symptom burden accounting for up to 39%–46% of the impairment in health-related quality of life (4,5,30).

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**Figure 1.** Integration of palliative care within the care process.
Unfortunately, pain and other symptoms are typically not recognized by renal clinicians (32) and remain under-treated. Routine symptom assessment is, therefore, integral to quality ESRD care.

Three global symptom screening tools have been validated in ESRD: the modified Edmonton Symptom Assessment System (4,5,30), the Patient Outcome Scale renal symptom module (33), and the Dialysis Symptom Index (34). Renal programs in Canada and the United Kingdom are currently using the Edmonton Symptom Assessment System and Patient Outcome Scale, respectively, to systematically identify ESRD patients who may benefit from interventions. Given the minimal burden to patients and staff, assessments can be completed by patients with nurse facilitation routinely during clinic visits for predialysis and home dialysis patients and with monthly review of dialysis patients.

In December of 2008, the United Nations Special Rapporteur on the Right to Health and the Special Rapporteur on Torture stated that adequate pain management should be regarded as a basic human right (18). Although attitudes of nephrologists to chronic opioid use is not known, 72%–84% of ESRD patients with significant pain have no analgesia prescribed (35). The prevalence of analgesic use in ESRD is highly variable but estimated at 24% (36). Approximately 15% are prescribed opioids, and even acetaminophen use is low at 6%.

One of the major barriers to effective pain management is the fear of opioid addiction from the perspectives of both patients and physicians (37); 35% of family physicians reported that they would never prescribe opioids for moderate or severe chronic pain, identifying addiction as a major barrier (38). Short-term opioid treatment for acute pain is associated with negligible addiction rates (0.03%–5%) (39). The prevalence of opioid abuse may be as high as 20% in patients receiving opioids for chronic pain (37). However, the recent increase in abuse of opioids is predominantly in young adults ages 18–25 years (37). Studies of older patients attending specialty clinics found rates of 1%–3% (40). There are no data specific to ESRD patients.

Addiction is characterized by loss of control over use, continued use despite knowledge of harmful consequences, compulsion to use, and craving (the four Cs). Aberrant drug behaviors, commonly used to identify addiction, refer to drug use that is not medically sanctioned (such as dose escalation, running out of drug early, binging, sharing of pain pills with relatives or friends, and doctor shopping to obtain multiple prescriptions). Diagnosing opioid addiction in ESRD patients is hampered by a lack of data on which aberrant behaviors best predict drug abuse. Aberrant behaviors may be precipitated by patients’ untreated pain, depression, anxiety, and maladaptive coping strategies, common issues for ESRD patients (41,42), rather than by addiction. In fact, nonaddicted patients frequently misuse opioids (43). The only major difference differentiating dialysis patients with chronic pain and patients with addiction is that patients not addicted are not seeking a psychoactive effect from their drugs.

Perhaps a more pressing concern for clinicians prescribing opioids for patients with limited life expectancy is the increased risk of death from unintentional drug overdoses (44). Most opioid deaths are accidental, and about one-half of the patients have a medical history of pain treatment (45). However, most patients who die from opioids are taking high daily doses and have one or more indicators of substance abuse as outlined above (45). Opioids are also one of a long list of medications that place the elderly at greater risk of falls, which constitute a leading cause of injuries, hospitalization, and deaths among the elderly (46). Although opioids have the potential to markedly improve patients’ symptom burden and quality of life, it is clear their use must be monitored carefully to prevent misuse and maximize benefit.
Evidence supporting the effectiveness of chronic opioid use in ESRD for chronic pain is extremely limited (47). Although opioids provide effective analgesia, they may exacerbate symptoms already prevalent in dialysis patients, such as cognitive impairment, sleepiness, nausea, vomiting, anorexia, and pruritus. Ongoing careful reassessment of the impact of chronic opioid use on overall symptom burden and functional status is essential. In addition, current guidelines (48,49) suggest universal precautions by screening for risk of abuse before starting opioids using a tool such as the Opioid Risk Tool (50). This tool identifies risk factors for opioid addiction, such as youth, current, past, or family history of substance abuse, psychiatric disorders, and childhood history of sexual abuse. Higher risk does not preclude opioid-based pain management but does require heightened monitoring for aberrant opioid behaviors. Management strategies for suspected opioid addiction or patients considered high risk for abuse or accidental death are outlined in Table 1. Frequent visits to the dialysis unit provide an ideal opportunity to coordinate and monitor outpatient use of opioids. Despite intravenous access, patients should be dosed orally whenever possible, even when on dialysis. Exceptions would include acutely ill patients compromised by factors such as vomiting, end-of-life weakness, or bowel obstruction.

The choice of analgesic for ESRD patients is very important. Active metabolites for many analgesics, including opioids, are excreted by the kidney, accumulate in patients with kidney failure, and may lead to toxicity. Recent reviews on the appropriate management of chronic pain in kidney failure and the evidence to support the use of particular analgesics (51–53) (Figure 3) have led to the development clinical algorithms based on an adapted World Health Organization Analgesic Ladder (Figure 4) (54), and they are increasingly being used by nephrology programs across North America and the United Kingdom. In addition, the United Kingdom has established renal-specific terminal symptom algorithms, including the management of terminal pain, as part of the Liverpool Care Pathway (55,56), an integrated end-of-life care pathway implemented across the United Kingdom.

Most ESRD patients have a neuropathic component to their pain (e.g., peripheral neuropathy, phantom limb pain, ischemia, calciphylaxis, carpal tunnel syndrome, or steal syndrome). Neuropathic pain is typically described as burning, shooting, or stabbing and may be associated with episodes of spontaneous pain, hyperalgesia, and allodynia. It is often poorly responsive to opioids, requiring doses that are associated with unacceptable toxicity. In such cases, the use of adjuvants, either alone or in conjunction with steps 1–3 analgesics of the World Health Organization analgesic ladder, is crucial to control pain and avoid high opioid doses. Tricyclic antidepressants and anticonvulsants are the two classes of drugs for which there is most evidence of efficacy (51).

Despite the challenge of managing chronic pain in dialysis patients, professional medical bodies expect physicians to have the knowledge, seek out the knowledge, or consult pain or palliative care specialists appropriately (57). Fears of opioid addiction cannot derail the right to receive adequate pain management. Clinical competence and scope of practice is not an acceptable reason to refuse to treat chronic pain or patients who are perceived to be otherwise difficult (57). Physicians, however, are under no obligation to provide medications that they feel are inappropriate.

### Table 1. Management of high risk of addiction or suspected opioid addiction

<table>
<thead>
<tr>
<th>Type of Patient</th>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>High risk of addiction (based on past or family history)</td>
<td>Check patient’s history of receiving controlled substances to ensure a single provider</td>
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<tr>
<td></td>
<td>Frequent dispensing (e.g., weekly)</td>
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<tr>
<td></td>
<td>Frequent pill counts</td>
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<tr>
<td></td>
<td>Avoid opioids with high potential for abusea</td>
</tr>
<tr>
<td></td>
<td>Keep dose below 300 mg/d morphine equivalentb</td>
</tr>
<tr>
<td></td>
<td>Consider methadone or buprenorphine treatment—both seem to be relatively safe for use in ESRD (Figure 3)</td>
</tr>
<tr>
<td></td>
<td>Regular urine testing (one to four times per month) for nonanuric patients and serum drug testing for anuric patients</td>
</tr>
<tr>
<td>Suspected opioid misuse/addiction</td>
<td>Consider referral to a chronic pain specialist</td>
</tr>
<tr>
<td>Currently addicted to nonopioid drugs</td>
<td>Opioids may be contraindicated—refer to a chronic pain specialist</td>
</tr>
</tbody>
</table>

*aOpioids considered to have a higher potential for abuse, such as hydrocodone and oxycodone, are not the recommended opioids for use in ESRD for reasons related to their increased risk for toxicity (Figure 3).

*bESRD patients rarely require doses greater than 300 mg/d morphine equivalent.
factors into clinically useful prognostic tools. There are limitations to each of these prognostic models, and no model addresses patients managed conservatively. As a result, no model has emerged as the most useful. Perhaps one of the more promising models is a recently developed prognostic tool for prevalent hemodialysis patients (58) that combines actuarial estimations from the presence of traditional risk factors of age, serum albumin, and two comorbidities (peripheral vascular disease and dementia) with the modified surprise question (SQ): would you be surprised if this patient were to die in the next 6 months? The intent of the SQ is to counter the tendency of physicians to overestimate prognosis by asking them to consider whether the patient’s death within 6 months is within the realm of possibility. The SQ has been found to be effective in identifying dialysis patients who are 3.5 times more likely to die within 1 year (59). This tool is available free online and as an application for handheld devices (60). The model also predicts 12- and 18-month mortality, although the accuracy of these predictions has not been determined. This tool is currently being used in pilot palliative care programs in several Canadian and United Kingdom renal units, and additional validation and refinement are ongoing. The simplicity of the model allows for relatively easy integration into routine dialysis care with limited staff burden. Poor predicted survival probabilities could be used as prompts for timely discussions of goals of care and determination of end-of-life care preferences through ACP.

The timing of end-of-life discussions is important given unpredictable illness trajectories and progressive cognitive decline in ESRD (61). Approximately 73% of dialysis patients have either moderate or severe cognitive impairment on formal testing despite no prior documented history of cognitive impairment (61). Early ACP with ongoing communication and re-evaluation throughout the illness trajectory is clearly important. Sentinel events, such as hospitalizations, acute illness, and decline in functional status, present additional opportunities to engage in ACP.

There is increasing recognition that dialysis may not be the best treatment choice for all patients, especially those patients with poor functional status and high levels of comorbidity (62–64). There is a role for conservative care for those patients with goals of care that are primarily palliative or patients who perceive limited benefit and considerable burden from dialysis (63–68). This finding is supported by current clinical guidelines (23,25). Conservative care focuses on slowing the decline in renal function, actively managing symptoms, using ACP, and providing appropriate palliative care to address patients’ goals of care and optimize their quality of life (68). The specifics of facilitating ACP within the context of ESRD have been reviewed recently in this Ethics Series (69) and elsewhere, and therefore, they will not be discussed here (70–72).

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**Table 3.** Preferred analgesic medication in ESRD.

<table>
<thead>
<tr>
<th>Medication</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Recommended</strong></td>
<td></td>
</tr>
<tr>
<td>Acetaminophen</td>
<td>Maximum daily dose of 3.2 g/day. In high risk patients limit the maximal dose to 2.6 g/day (chronic stable liver disease, alcoholics, and malnourished patients).</td>
</tr>
<tr>
<td>Hydromorphone</td>
<td>Hydromorphone-3-glucuronide (a toxic metabolite) accumulates without dialysis therefore this may not be an appropriate analgesic for patients with stage 5 CKD NOT on dialysis. Long acting Hydromorphone is relatively contraindicated in ESRD based on expert opinion, due to the narrow therapeutic window for opioid analgesic effect relative to toxicity.</td>
</tr>
<tr>
<td>Fentanyl Patch</td>
<td>Should not be started in opioid naïve patients</td>
</tr>
<tr>
<td>Methadone</td>
<td>Monitor QT by ECG.</td>
</tr>
<tr>
<td>Gabapentin</td>
<td>Titrated slowly; doses up to 600 mg/day are generally safe but monitor for side effects, especially with doses above 300 mg/day (nystagmus, ataxia, tremor, somnolence, and reduced level of consciousness).</td>
</tr>
<tr>
<td><strong>Use With Caution</strong></td>
<td></td>
</tr>
<tr>
<td>Oxycodone</td>
<td>Limited evidence of pharmacokinetic safety in CKD. Literature reports suggest no major concerns; has a higher potential for abuse than the above-recommended opioids.</td>
</tr>
<tr>
<td>Tramadol</td>
<td>Sustained release tablets NOT recommended in dialysis patients. Seizure with doses higher than 150mg daily in eGFR &lt; 30 ml/min a concern.</td>
</tr>
<tr>
<td>Nortriptyline/desipramine</td>
<td>Tricyclic antidepressants are alternatives to gabapentin although with higher risk for adverse effects.</td>
</tr>
<tr>
<td><strong>DO NOT USE</strong></td>
<td></td>
</tr>
<tr>
<td>Codeine, morphine, meperidine, propoxyphene</td>
<td>Neurotoxic metabolites that are renally excreted and that accumulate in chronic kidney disease with a high likelihood of toxicity.</td>
</tr>
</tbody>
</table>
Severe Pain (7 – 10)
Hydromorphone – start 0.5 mg PO q 4h + 0.5 mg PRN q 2h for breakthrough pain
± Nonopioid analgesics and Adjuvants

Moderate Pain (4 – 6)
Hydromorphone – start 0.5 mg PO q 4h PRN OR Tramadol 25 mg daily up to 75 mg bid.
± Nonopioid analgesics and Adjuvants

Mild Pain (1 – 3)
Acetaminophen
± Adjuvants (for neuropathic pain)

*Acetaminophen: Do not exceed 3.2 g/day of acetaminophen to avoid hepatotoxicity as per FDA recommendations. In high risk patients (malnourished, alcoholic) limit to 2.6 g/day.

@Adjuvants for neuropathic pain include antidepressants and tricyclic antidepressants.

PRN dosing for breakthrough pain: ~10% of the 24 hour dose of opioid prescribed every 1 to 2 hours as needed.

Severe pain: patients should be converted to a long-acting opioid or methadone once a stable hydromorphone dose has been achieved, with PRN doses of hydromorphone made available.

A bowel regimen to prevent constipation, which is an anticipated adverse effect of opioids, should accompany all opioid prescriptions.

Figure 4. Modified analgesic ladder for chronic pain management in patients with ESRD.

Model for Delivering High-Quality Palliative Care

Several key components are required to deliver high-quality palliative care. This discussion will focus on timely access to palliative care services, including consultation with specialist palliative care, a multidisciplinary team to manage the physical, psychosocial, and spiritual end-of-life needs of ESRD patients, adequate nephrology fellow training in palliative care, and patient and family education.

Most ESRD patients will experience substantial disability, symptom burden, and requirement for quality palliative care beyond the last year of life (73,74). Traditional palliative care models have focused primarily on cancer patients, many of whom experience most of their symptoms and disability in the last 6 months of life. Models limiting access to palliative care services, such as hospice, based on this understanding of illness do not adequately serve the needs of ESRD patients.

Patients should be offered the option of dying where they prefer, including at home with hospice care, provided that there is sufficient and appropriate support to enable this process. Although hospice is recognized for providing excellent end-of-life care, few ESRD patients receive hospice care, even after withdrawal from dialysis (19). Using the United States Renal Data System, it was determined that only 13.5% of 115,239 dialysis patients in the United States who died between January 1, 2001, and December 31, 2002 used hospice. Patients who used hospice services were more likely to die at home. Decreased hospitalization costs led to substantial cost savings (19). In oncology, receiving early palliative care is associated with better quality of life, fewer emergency department visits and hospitalizations, less aggressive care at the end of life, and surprisingly, longer survival (75). Early integration of palliative care, including the creation of conservative care pathways, and access to specialist palliative services, such as hospice, are likely to be hugely beneficial to ESRD patients.

Renal palliative care is best delivered through the combined expertise of nephrology professionals, family or community-based professionals, and specialist hospice or palliative care providers (23). Specialist palliative care consultation might be required for the four following reasons: (1) complex pain and symptom control, (2) psychological or family/social issues despite first-line intervention by the renal team, (3) when conservatively managed patients are approaching the last few weeks of life, especially if home care is preferred by the patient, or (4) when patients and family are experiencing difficulties in the decision to start or stop dialysis despite open discussion with the renal team, particularly when there are issues of family conflict, impaired capacity, or complex concurrent disease.

Renal palliative care requires a multiprofessional team with expertise in managing not only the physical, psychologic, and social needs but also the spiritual aspects of end-of-life care for ESRD patients (23). This aspect might include chaplains or spiritual counselors. ESRD patients have substantial unmet spiritual care needs (9) that impact negatively on their quality of life (76). Many report a fear of being a burden and becoming dependent on others or a loss of dignity, self-esteem, or control. These losses often evoke deeper questioning about meaning and spiritual beliefs. Providing spiritual support is a core component of comprehensive palliative care and may help to preserve or enhance quality of life, even in the face of life-limiting illness. Simple screening questions, such as are there any spiritual concerns you would like to have addressed or discussed with a member of the healthcare team?, may help initiate more in-depth discussions for those patients who indicate distress. Support should also be offered to patients’ families, including bereavement support where appropriate (23).

Professionals delivering care should receive training in assessment and management of symptoms and advanced communication skills (23). Training in palliative care for nephrology trainees is inadequate. One-third of fellows had conducted two or fewer family meetings, and specific palliative care content areas, such as pain management, communicating bad news, and how to access palliative care services, were taught infrequently. What little palliative care training was received frequently occurred without attending nephrologist supervision (77). It is not surprising, therefore, that nephrologists do not feel adequately prepared to deal with end-of-life issues for their patients (24). There is clearly a need to upgrade training to enable delivery of high-quality palliative care.

Inadequate patient education is also a barrier to effective integration and delivery of palliative care. In Canada, approximately 60% of individuals 16 years and older lack the capacity to obtain, understand, and act on health information and services and make appropriate health
decisions on their own (18). Health illiteracy is even more prevalent among those patients with ESRD. Most ESRD patients have poor knowledge of palliative care (10), thinking that it is solely for cancer patients or that it is equivalent to terminal care or giving up on life. The benefits of palliative care need to be emphasized to patients, along with the understanding that palliative care is not so much about dying but about living the days that one has left to the maximum.

Summary
Ultimately, the responsibility of caring for ESRD patients and treating their symptoms, whether these symptoms are related to ESRD or comorbid diseases, is with the nephrology team. Nephrology programs need to develop and integrate a palliative care strategy for ESRD patients. This strategy must include education of nephrology trainees and the multidisciplinary team as well as patients. Ongoing research and knowledge translation will continue to be central to this process. Given the cost to patients (in terms of symptom burden, poor quality of life, hospitalizations, and burden of life-sustaining treatment) and the costs to healthcare systems, systematically incorporating palliative care into the management of ESRD patients is imperative.

Disclosures
None.

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