End-stage kidney disease

The last 12 months

CPD

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Background
Chronic kidney disease (CKD) is increasingly prevalent in Australia's ageing population. Over the past decade, there has been growing recognition that dialysis does not benefit every patient with end-stage kidney disease (ESKD). Patients with advanced age, significant comorbidities and poor functional status may not gain a survival benefit with dialysis when compared with being managed conservatively. These developments have implications for general practitioners (GPs). A further development has been the emergence of renal supportive care, a patient-centred approach that integrates the principles of palliative care into nephrology.

Objective
The aim of this article is to outline salient aspects in the care of patients with ESKD.

Discussion
Salient aspects throughout the trajectory of ESKD are discussed, including symptoms of CKD, relevant management, prognostication, advance care planning discussions and end-of-life care. The role of the GP is vital, and it is recommended that GPs are involved early in a patient's CKD trajectory.

CHRONIC KIDNEY DISEASE (CKD) is increasingly prevalent in Australia's ageing population. End-stage kidney disease (ESKD), defined as an estimated glomerular filtration rate (eGFR) of <15 mL/minute/1.73m^2, can be managed by three pathways: dialysis, kidney transplantation or conservatively, without dialysis. In the modern era, nephrology has seen several important developments. First, a growing recognition that dialysis does not benefit every patient with ESKD. Patients with advanced age, significant comorbidities and poor functional status may not gain a survival benefit with dialysis when compared with being managed conservatively.[1,2] Second, and as a corollary of the first, an acknowledgement that, for many patients in the cohort described, the conservative care of patients with ESKD is both appropriate and preferable. Third, the creation of renal supportive care (RSC) services within departments of nephrology. RSC is a patient-centred approach that integrates the principles of palliative care – including symptom assessment and management, prognostication and advance care planning – into nephrology.[3] Each of these developments is relevant to general practice in the care of patients with ESKD, whether or not the patients are on dialysis.

Broadly, patients with ESKD in the final 12 months of their life are either: 1) being managed on dialysis or 2) on a conservative, non-dialysis pathway.

How is it determined that a patient with ESKD is entering the last 12 months of their life? Prognostication is notoriously difficult. Nevertheless, some factors have been statistically correlated with a poor prognosis in patients on dialysis: older age; increasing number of comorbidities, especially ischaemic heart disease and congestive heart failure; malnutrition and poor functional status.[4,5] In addition, a clinician's answer of 'no' to the 'surprise question' – 'Would you be surprised if this patient dies within the next year?' – has also been correlated with poor prognosis.[6]

For patients on a conservative pathway, survivorship may be longer than conventionally thought. An Australian study found that mean survival from eGFR <15 mL/min/1.73m^2 was 13 months in patients managed conservatively.[2] The signs that patients in this cohort are entering the final two months of their lives are: a significant deterioration in functional status, increasing symptoms and an increase in palliative care needs.[7]

The decision to pursue conservative, non-dialysis management for ESKD is an individualised choice based on many

factors other than survival, including patient-centred priorities, impact on one's function and family, and quality-of-life considerations. As patients managed conservatively have many months, and potentially years, of life remaining, they require active medical treatments of CKD complications, particularly those that may adversely affect quality of life. It is important that hospital-based nephrology units, community-based general practitioners (GPs) and allied health professionals work collaboratively to support these elderly, medically complex patients at each stage of their illness trajectory. Care coordination, best done by a dedicated renal nurse in conjunction with the patients' GP, is critical to ensure that care is not fragmented, and that available local resources are being maximally used. Furthermore, the cost of providing a conservative care program is relatively small when compared with the high yield of good health benefit.

Team members and their roles

The members of a clinical team caring for patients with ESKD and their respective roles include the following.

Nephrologist

The nephrologist initiates and coordinates all aspects of renal medicine. This includes decision making regarding commencing and withdrawing from dialysis; the management of complications of dialysis; preservation of residual renal function; and control and management of blood pressure, fluid status, calcium and phosphate metabolism and the effects of low levels of erythropoietin.

Renal supportive care service

In the modern era, a growing number of nephrology departments include an RSC service. RSC teams have a broad responsibility, as described previously. Members of the team consist of palliative care and renal physicians, clinical nurse consultants, social workers and dietitian support.[4] GPs could enquire with their local nephrology units whether an RSC service exists in their areas and, if so, how the GP and RSC could work together in the care of their patients. Where possible, joint care between GPs and RSC provides an ideal framework for good patient care in these cases. For patients who remain well, it is important to maintain regular contact at least every 2–3 months to ensure that early symptoms are promptly addressed and that patients feel supported. More frequent reviews, potentially weekly or more, are required for patients who are deteriorating, have high symptom burden or acute intercurrent illnesses, or are approaching the end of life. Clinicians interested in further reading can be referred to the St George Renal Service RSC guidelines (https://stgrenal.org.au/guidelines-and-policies/guidelines/renal-supportive-care).

Palliative care services

In addition to RSC services, general palliative care services may be involved in the care of patients with ESKD in hospital, in-patient palliative care unit and community settings. These settings may be the location of the deterioration and death of ESKD patients. In the absence of RSC services, palliative care services may be sole source of palliative care expertise.

General practitioners

GPs have a crucial role. Some patients may have known their GPs for years prior to referral to the relevant specialist and have a valuable therapeutic relationship. Other patients may not be aligned to one GP or practice. Where specialties such as nephrology, geriatric medicine and palliative care are involved, general practice has a critical role in managing specific medical issues, explaining to patients the details of their care, liaising between specialties, placing the disease in the context of the life of the patient, preparing patients and families for deterioration and death, and, occasionally, needing to advocate for patients. There may be a spectrum of involvement by the GP in these aspects of care. For some patients, the nephrologist has the predominant role, and communication with and from the renal unit is vital. For others, the GP holds the predominant responsibility for the aforementioned aspects of care.

The pathways of care in the last 12 months

In their final 12 months of life, patients with ESKD are either on a dialysis or a conservative, non-dialysis pathway.

For patients on dialysis, the circumstances of their death generally fall into one of the three following categories:

- Death following a period of general deterioration, often marked by frequent hospitalisation.
- A sudden death, usually from cardiovascular causes.[8,9] Any sudden death can have a profound effect on bereavement, not just on the family, but also on clinicians and fellow patients, particularly in a dialysis unit.
- Death following withdrawal from dialysis. This is a common cause of death in ESKD.[10] As Swidler noted: 'Although dialysis is life-sustaining therapy ... it may also create, increase or prolong suffering while not restoring or maintaining well-being, function or cognition'.[11] Reaching a point in the trajectory of ESKD where active treatment, including the process of dialysis itself, becomes more burdensome and less sustainable is a matter of clinical judgement and negotiation with the patient. Withdrawal decisions are often made in the context of either progressive reduction in quality of life or an acute medical complication.[12,13] Withdrawing treatment that is considered no longer beneficial to the patient is ethically and legally valid. It is neither suicide nor euthanasia, nor does it constitute medical abandonment. The truth of that statement is upheld where there is careful and sensitive communication, coupled with an active pursuit of comfort and appropriate management of the post-withdrawal phase leading up to the patient's death.[4] The duration between withdrawal and death varies. For patients who are anuric, the median time to death is approximately seven days.[12,14] For those patients still passing urine, as many patients on dialysis do, this period may be weeks to a few months.[14]

Death on a conservative pathway

The decision to manage ESKD conservatively may be reached by patient consultation with a nephrologist, geriatrician or general practitioner. It is important that family members and loved ones are involved in these discussions, as they may mistakenly perceive conservative management as substandard. Conservative management should not be viewed as abandonment or substandard care. It may mean that elderly patients avoid the suffering that can come from dialysis in some cases. The family's awareness of such discussions may also prove crucial in situations in which the patient is cared for by doctors who are not part of their regular medical team. Patients with ESKD should ideally be managed in a system where there is constant oversight by one clinician who is familiar with that patient. Symptoms and management for those on a conservative pathway are outlined in Tables 1 and 2.

The trajectory of ESKD that is conservatively managed is often one of relatively preserved functional status until late in the course of illness, which is characterised by a rapid decline towards death.[7] Initially, when the patient has relatively preserved functional status, management focuses more on CKD. Angiotensin converting enzyme inhibitors or angiotensin receptor blockade medications are often continued with the intention of protecting kidney function if they will also enhance quality of life and/or help a patient achieve their goals.[15] Although the patient is not undergoing dialysis, the nephrologist should continue to care for their conservatively managed patients. No dialysis does not mean no treatment, and it is important to emphasise this to the patient and their family. Actively treating the complications of ESKD can improve quality of life and improve the symptom burden.[4] This may include management of anaemia (with erythropoietin-stimulating agents), CKD–mineral and bone disease and hypertension; fluid management; CKD-specific nutritional interventions with a focus on avoiding malnutrition and improving quality of life; and specific considerations regarding medication dosing in CKD. In the second, more rapid phase of terminal uraemia, comfort takes precedence in the last weeks or days of life.[15]

Palliative care: Early and late

There are several key elements in the supportive care of patients with ESKD leading up to the terminal phase. Ideally, all clinicians involved can contribute to the following elements.

Symptom management

Symptoms are common in ESKD. Symptoms and their management will be discussed in two parts. The first part outlines the common symptoms experienced by patients with ESKD (Tables 1 and 2); the second outlines the specific symptoms of the terminal phase (Box 1). ESKD alters the pharmacokinetics of renally eliminated medications, leading to a risk of accumulation and toxicity. Dose adjustments will generally be required.[16]

Table 1. Common symptoms in patients with end-stage kidney disease and their management – Part 1: Fatigue and pain[4,15,16]

Symptom	Suggested management
Fatigue	• Exclude and treat contributing factors such as sleep disorders, anaemia, nocturnal symptoms (refer to Table 2), vitamin D deficiency, metabolic acidosis, tertiary hyperparathyroidism, hypothyroidism, mood disorders • Good nutrition • Regular exercise at any tolerated level • Cognitive and psychological approaches (eg relaxation therapy) • Practical energy conservation strategies, such as sitting whenever possible to do activities of daily living such as cooking and bathing, pre-scheduled frequent short rest periods
Pain	**Non-pharmacological** • Heat and cold packs or liniments for localised pain • Physiotherapy and/or hydrotherapy for chronic musculoskeletal pain **Pharmacological** Management of pain should be guided by the usual management of various pain syndromes (eg acute gout, osteoarthritis or diabetic peripheral neuropathy). These treatments should then be adjusted to ESKD and, where relevant, dialysis. When there is doubt, nephrology, RSC or pain medicine physicians should be consulted. Where opioids are appropriate, proceed stepwise from non-opioid analgesics to weak opioids and strong opioids. • Mild pain – Non-opioids such as paracetamol (up to 3 g daily); avoid systemic NSAIDs – For localised pain, consider topical NSAIDs (eg diclofenac gel 5% or 10%) twice daily or three times daily • Moderate pain – Tramadol with dose reduction to 50 mg twice daily (maximum) • Severe pain – Opioids (avoid morphine as its metabolites will accumulate in ESKD); suggested opioids include hydromorphone 0.25–0.5 mg every four hours orally, oxycodone 2.5–5 mg every four hours orally and buprenorphine patches weekly, starting at 5 µg/hr transdermally • Adjuvant therapy – Gabapentinoids, tricyclic antidepressants

ESKD, end-stage kidney disease; NSAIDs, nonsteroidal anti-inflammatory drugs; RSC, renal supportive care

Table 2. Common symptoms in patients with end-stage kidney disease and their management – Part 2: Other symptoms[4,15,16]

Symptom	Management
Sleep disturbances	• Exclude and treat contributing factors such as sleep apnoea, restless legs syndrome or pruritus • Sleep hygiene
Restless legs syndrome (RLS)	**Non-pharmacological** • Exclude contributing factors – iron deficiency anaemia, dopamine antagonists (eg metoclopramide) • Intradialytic exercise (pedals at base of dialysis chair) **Pharmacological** • Gabapentinoids – If on dialysis – gabapentin 100 mg or pregabalin 25 mg after each dialysis session – If not on dialysis and estimated glomerular filtration rate (eGFR) <15 mL/min/1.73m^2 – gabapentin 100 mg or pregabalin 25 mg every second night – If eGFR >15 mL/min/1.73m^2 – gabapentin 100 mg or pregabalin 25 mg every night • Dopamine agonists – Ropinirole 0.5 mg at night – Pramipexole 0.25 mg at night
Pruritus	• Exclude and treat contributing factors – secondary hyperparathyroidism, hyperphosphataemia, allergies or contact dermatitis, dry skin, scabies • Good skin care – Moisturisation – Avoiding long hot showers and harsh soaps • Gabapentinoids – refer to dosing regimen for RLS • Evening primrose oil 1–2 capsules twice daily • Menthol topically • Ultraviolet B therapy
Nausea	• Exclude and treat contributing factors such as constipation, gastroparesis, medications (opioids, dopamine agonists and antidepressants) or taste changes • Small frequent meals • Encourage relaxed, upright position after eating to facilitate digestion • Good oral hygiene • If patient has RLS – avoid dopamine antagonists (metoclopramide, haloperidol) – Use domperidone 10 mg before meals and at night • If no RLS, then dopamine antagonists can be used – monitor for RLS that may be precipitated – Metoclopramide (5–10 mg three times per day before meals) also has prokinetic effects and can be useful if gastroparesis is a contributor – Haloperidol 0.5 mg twice daily – Cyclizine 12.5–25 mg three times per day before meals

Advance care planning

Advance care planning is a process of communication, understanding, and discussion between a patient, their caregivers and healthcare providers, with the goal of clarifying values and preferences for future care, including care at the end of life.[17] It is important for patients with ESKD, who often have multiple comorbidities, to understand their prognosis, make decisions about their future care and communicate their wishes to their caregivers and healthcare providers so that their wishes can be respected and adhered to when the patient becomes critically unwell. Advance care planning is endorsed by Australian[4] and international guidelines[18] and legally recognised in all Australian jurisdictions. An advance care plan for a patient with ESKD should include a preference to avoid invasive treatments such as intubation and cardiopulmonary resuscitation; instructions regarding initiation, withholding and/or withdrawal of dialysis; and preferred place of death. Advance care planning discussions should be recorded and provided to all healthcare providers involved in the patient's care. It is recommended that doctors (GPs or nephrologists) initiate these discussions as this takes the burden from patients and their families.

Palliative care: Terminal care of the dying patient with ESKD

Although most patients with CKD prefer to die at home or in a hospice,[19] only 10% of patients with CKD ultimately die at home.[20] Early knowledge that this is a patient's wish is essential.[4] If home is the location of care, the role of the GPs is critical in patient care, liaising with community palliative care and RSC services, and emotionally supporting the family through this period and into their bereavement. Planning for end-of-life care at home requires expertise and careful coordination. Ideally, there is sufficient carer support available. Even with the best planning, a complex clinical scenario may overwhelm a family, and death may need to occur in an institutional setting. Reassuring the family that they have done

Box 1. The physical care of the dying patient with ESKD[4,15]

- A single room for the privacy and intimacy of the family.
- A pressure mattress.
- Meticulous mouth care – cotton wool sticks dipped in water and used to clean the oral cavity or a dry mouth spray can be useful. For both, encourage families to participate in this care.
- If the patient continues to pass urine, consider an in-dwelling catheter as a comfort measure.
- When the patient is sleeping for longer periods with reduced oral intake, ceasing oral medications or converting necessary medications to a subcutaneous route.
- Symptom management in the dying patient:
  - Pain – it should never be assumed that an unconscious patient does not experience pain. Ask the nursing staff or family if there are any signs of pain (groaning or grimacing) on being turned in bed. When present, continue background opioids in subcutaneous or transdermal form. Avoid morphine as its metabolites will accumulate in ESKD and use hydromorphone instead (starting dose of 0.25 mg subcutaneously every four hours).
  - Terminal agitation – use midazolam (starting dose of 2.5–5 mg subcutaneously every four hours or equivalent dose in a syringe driver). If not settling, escalating dose to match the severity of agitation.
  - Terminal secretions – reposition patient. If not settling, use glycopyrrolate 400–800 µg subcutaneously every hour.
- Symptoms common in the dying patient with ESKD:
  - Uraemic encephalopathy – this manifests as drowsiness through to coma. Patients may exhibit uraemic jerks. For the latter, use either clonazepam drops 0.25–0.5 mg sublingually or subcutaneously, or midazolam 2.5 mg subcutaneously.
  - Nausea – if the patient has a history of restless legs syndrome, avoid metoclopramide or haloperidol as they are dopamine antagonists and may worsen this. Use cyclizine 25–50 mg three times per day subcutaneously.

their absolute best is important, as transfer from home can trouble families at this time and in their bereavement. A hospice or palliative care unit can be alternative locations for end-of-life care, and they are able to provide medical support, nurses, social workers and pastoral care. Linking to an RSC service may help in facilitating admission to a palliative care unit when patients are approaching the end of life.[1]

In practical terms, the important elements of care for a patient dying with ESKD include physical care and support for family.[4]

Physical care includes careful symptom assessment, appropriate charting of regular and as-needed comfort medications, bladder and bowel care and pressure area care (Box 1). It is critical that symptoms are not only treated when they occur but also planned for ahead of time.

All clinicians involved in the care of a patient who is dying have a responsibility to communicate clearly and compassionately to the family. Communication should include an explanation of what is occurring and what may occur in the terminal phase, and link descriptions of anticipated symptoms with anticipated management. For families of patients who have withdrawn from dialysis, it is important to reassure them that this choice is reasonable and ethical and does not constitute suicide or euthanasia. Finally, it is important to encourage families to rest, eat and drink, support each other and share the responsibility of this period of vigil leading to the death. A social worker can be invaluable in this regard. The spiritual needs of patients, including religious support or pastoral care, if indicated, should always be considered as part of care of the dying patient.

Bereavement

The GP can also have a vital role in supporting the family in bereavement. The palliative care service or local RSC service will often have access to social workers or information regarding bereavement counselling services available.

Conclusion

The care of patients with ESKD, up to and including the final year of their lives, requires a careful and respectful coordination of the relevant specialist services and general practice. The needs of patients and their families may be complex. For patients on dialysis, the locus of care is often the dialysis centre and the nephrology team. For all patients with ESKD, nephrology, RSC and general practice have an important role. GPs usually have known the patients and their families for much longer than the specialty teams, and therefore can contribute greatly towards advance care planning and holistic ongoing care. Symptom management should be a coordinated effort between the GP and the relevant specialist services. By initiating advance care planning early in the course of CKD and providing supportive care to all patients, health practitioners can work as a team to help improve the quality of life of all patients with renal disease throughout their disease trajectory, as well as supporting them in the end-of-life period.

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Competing interests: None.

Funding: None.

Provenance and peer review: Commissioned, externally peer reviewed.

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