Chapter 14
Dialysis Versus Conservative Care in the Elderly: Making a Choice

Aine Burns

Introduction

The aging process results in marked alterations in the kidneys, impairing their ability to maintain homeostasis, adapt to changing local environments and recover from injury. These changes are both anatomical and functional and have been considered the cause of the increased propensity of the elderly to acute or chronic renal failure that may be accelerated and/or accentuated by diseases such as diabetes mellitus and hypertension.

Frailty is a biologic syndrome of decreased reserve, and resistance to stressors that results from cumulative decline across multiple physiologic systems is common in elderly CKD patients. Protein-energy wasting (PEW), sarcopenia, dynapenia, etc., which accompany frailty, contribute to poor outcomes.

One of the biggest challenges nephrologists face is how to best serve frail elderly and (increasingly) very elderly patients who present with advanced CKD.

Perhaps the most important thing to recognise from the outset is that each individual patient presents with his or her own unique set of social, medical and cognitive as well ethical and moral circumstances requiring multiple and individually tailored solutions.

A further consideration is the changing nature of this field as populations survive even longer and patient and public expectations adjust accordingly. Arguably, nephrology has become the victim of its own success as renal replacement therapy has become technically possible even in the sickest patients [1].

Yet, despite anecdotal success stories, there are numerous elderly people for whom dialysis has not been a success, where symptom burden and quality of life is

A. Burns, MB, BaO, Bch, MRCPI, MD, FRCP, MSc Med Ed
Department of Medicine, Centre for Nephrology, University College London,
Royal Free NHS Foundation Trust, London, UK
e-mail: aine.burns@nhs.net

M. Misra (ed.), *Dialysis in Older Adults: A Clinical Handbook*,
DOI 10.1007/978-1-4939-3320-4_14

poor and death may even have been hastened and certainly medicalised. The number of patients withdrawing from dialysis programmes bears witness to this fact. These latter considerations have led many clinicians to offer a structured alternative 'conservative or supportive care' to elderly patients with advanced CKD. In recent years, the success of these endeavours has enshrined 'conservative care' (CC) as a legitimate alternative to haemo- or peritoneal dialysis, particularly for the frail older patient. This chapter will explore the current evidence clinicians can draw upon to help inform an individual patient's choice and deliver optimal non-dialytic or conservative care (CC).

Historical Perspective

Since the introduction of chronic dialysis in the 1960s, there has been increasing demand fuelled by technical success, medical advances and increased patient and public expectation. In the early years of chronic dialysis, treatment was unashamedly rationed with young, otherwise healthy, candidates, or those with dependent families being chosen amongst the lucky few to receive treatment! Throughout the 1980s and 1990s, increasingly older patients were commenced on dialysis, many with very significant additional co-morbidity. Crude survival amongst these patients was shockingly poor: as bad or even worse than many advanced cancers. Furthermore, these patients were found to suffer a considerable burden of physical symptoms [2], and many authors reported a marked and permanent deterioration in functional status and quality of life (QOL) after dialysis initiation [3]. Thus, many nephrologists have questioned the wisdom of offering dialysis to all comers. It has been suggested that a conservative approach might be a more humane way to deal with advanced CKD in elderly patients, particularly in those with poor functional status and multiple other co-morbidities. Over the past decade, there has been a growing wave of interest in CC both in palliative and geriatric care communities and amongst nephrologists [4, 5]. Conservative and end-of-life care together with symptom management are now included on the curriculum for nephrology trainees on both sides of the Atlantic. Today, most renal units in the developed world aspire to deliver symptom-driven multidisciplinary care to their elderly patients with an increasing realisation that the removal of waste solute and water, alone, is not the answer. In recent years, the take-on rates for dialysis programmes have plateaued in many European countries. However, it is not known what part the emergence of CC has played in this change.

Terminology for Non-dialytic Management

There is no consensus regarding terminology for these latter approaches. Table 14.1 outlines the commonly used terms. For the purposes of this chapter, we will use the term conservative care (CC).

Table 14.1 Terms used for non-dialytic conservative therapies

Conservative management
Conservative care
Maximum conservative management
Renal supportive care
Residual renal support
Palliative renal care
Conservative kidney care
The non-dialysis option
Structured supportive care

This varied terminology reflects significant differences in approaches to care for patients who either do not wish to receive dialysis or are deemed not suitable and therefore are not offered renal replacement therapy. Treatment pathways vary as well. On one hand, patients may be discharged back into the community with no renal follow-up with the label 'unsuitable for dialysis'. On the other hand, intensive patient and family education regarding treatment options, prognosis and complications are offered with shared decision-making and follow-up by renal services. Such programmes usually include anaemia management, symptom control, treatment of intercurrent illnesses and a package of social and supportive services that can be escalated as the patient's condition deteriorates. Some programmes also strongly encourage patients to create advance directives or other formal end-of-life plans.

The existing terminology does not define whether a plan for CC was initiated by the patient alone, with their families or on the recommendation of a nephrologist or other health professional. Very few registries exist to catalogue CC patient outcomes. Similarly, the motivation behind CC decisions is rarely recorded and has only been investigated in a handful of very small studies.

Dialysis Choices

The choice of dialysis treatments for elderly patients has broadened in recent years. Regular haemodialysis (HD) is performed for the most part in the same manner as for younger patients. Conventional peritoneal dialysis (PD) performed four times daily by the patient or a family member at home can now be replaced by overnight or automated peritoneal dialysis (APD) systems and more recently, in some countries, by assisted peritoneal dialysis (see chapter on PD).

Conservative Care Versus Dialysis

Dialysis places a significant burden on elderly patients, their families and health service. There is evidence that elderly HD patients experience an increased rate of deterioration in functional and mental capacity on haemodialysis and have a

symptom burden and quality of life comparable to patients with advanced cancer. By contrast, many patients who choose a CC approach appear to have a fairly flat functional trajectory until a short time before death. Symptom burden in both groups has been shown to be high and may not differ significantly between patients undergoing dialysis and CC. Yet, impressive survivals have been documented in both cohorts of patients who commenced dialysis over the age of 80 years [6] or followed CC programmes [4].

Trajectories of decline in renal function vary hugely and often unpredictably with many elderly patients having a very slow decline and surviving with minimal (<5 ml/min) measured creatinine clearance. Thus, the boundaries are unclear as to when dialysis confers overall benefit. There are no controlled trials of CC versus dialysis, but several authors have attempted to determine whether dialysis significantly prolongs life in the old and frail. Current evidence suggests that although dialysis may extend survival, the number of out-of-hospital intervention-free days does not differ much between the two groups [7] and the survival benefit disappears as co-morbidity increases and functional status declines [4]. A convincing argument in favour of CC in patients over the age of 80 with high co-morbidity or poor functional status purely on the grounds of survival benefit has been put forth [8]. CC patients are also more likely to die at home or in a hospice than in an acute hospital setting. It is not clear whether dialysis improves symptoms or quality of life or merely exchanges one set of symptoms for another in the frail and elderly. Given the same education and free choice, older frailer patients choose CC [9]. Interestingly, there is also some evidence to suggest that survival curves diverge between groups of patients who choose CC compared with dialysis at relatively high e-GFRs, i.e. well before dialysis is initiated.

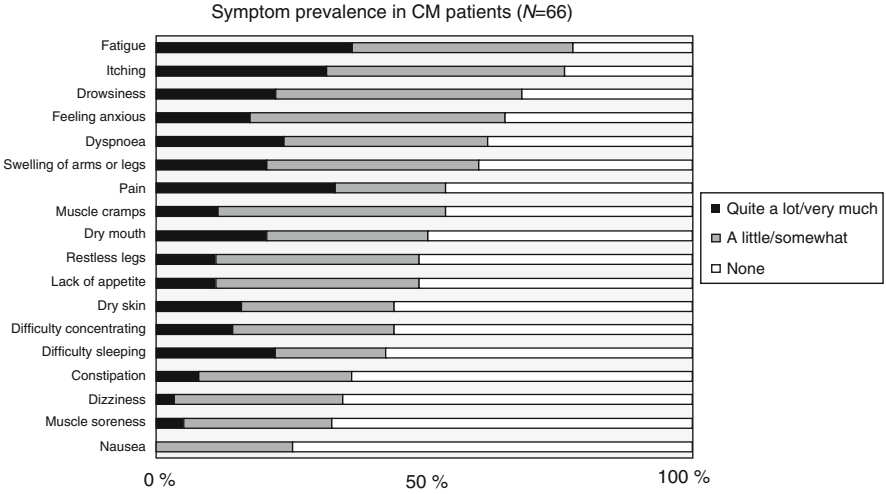
Symptom Prevalence in CC Patients

Elderly patients with advanced CKD and multiple co-morbidities have been shown to have high symptom and depression scores in cross-sectional studies. However, little is known about symptom trajectory over time and the effect of interventions such as dialysis. Detailed measurements of symptom burden are cumbersome and impractical for routine use in all patients. Table 14.2 reports the symptom prevalence in a cohort of CC UK patients [2].

Survival and Quality of Life

There are no randomised trials to determine whether elderly patients who choose dialysis over CC survive longer. It is unlikely that such studies will be undertaken for ethical reasons. However, there are several studies that catalogue the outcomes of elderly and very elderly patients on dialysis. Very impressive survival (median survival 46.5 months, range 0–107) has been reported by some for those who

Table 14.2 Symptom Prevalence in Conservatively Managed CKD patients [2]



initiated dialysis in their eight decade [6]. Registry data, however, would suggest that elderly people, particularly those with poor functional status and multiple co-morbidities, fare poorly with very many surviving less than 6 months on dialysis. A few studies have compared survival between patients undergoing dialysis and CC [4]. However, all studies are flawed by possible selection bias of healthier younger patients for dialysis intervention. Many authors have questioned whether such dialysis interventions are merely prolonging dying rather than extending meaningful life. Carson et al. who retrospectively examined survival and hospitalisation in a single unit's population of over 75 year olds found an increased survival in those dialysed but reported that almost every day of life gained was at the expense of a day spent in a hospital environment either on dialysis or as an inpatient [7]. Murtagh et al. reported that 1- and 2-year survival rates were 84 and 76 % in a group of patients opting for dialysis ($n=52$) and 68 and 47 % in those on a CC pathway ($n=77$) [10]. However, the survival advantage was lost in those patients with high co-morbidity scores, especially when ischemic heart disease was present. Da-Silva has recently reported that CC patients in their unit were older, more dependent and more highly co-morbid, had poorer physical health and higher anxiety levels than those choosing dialysis. Mental health, depression and life satisfaction scores were similar even when examined longitudinally. They also demonstrated that quality-of-life measures except life satisfaction decreased significantly after dialysis initiation but remained stable in CC patients. Their model, which controlled for co-morbidity, Karnofsky performance scale, age, physical health score and propensity score, confirmed an increased survival in HD patients (median survival from recruitment: 1317 days in HD patients (mean of 326 dialysis sessions) and 913 days in CC patients). Therefore, they concluded that patients choosing CC did not live as long as their counterparts on dialysis but maintained a better quality of life. Adjusted median survival from recruitment was 13 months shorter for CC patients than HD

patients [9]. Likewise, Hussain found a survival advantage for their patients who chose dialysis over CC, but this disappeared in the older frailer patients [8]. Whether post-dialysis initiation rehabilitation interventions would improve quality of life or longevity in this elderly co-morbid group is not known.

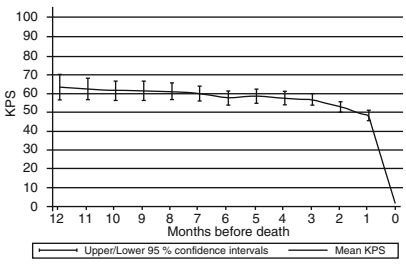
The Trajectory of Illness

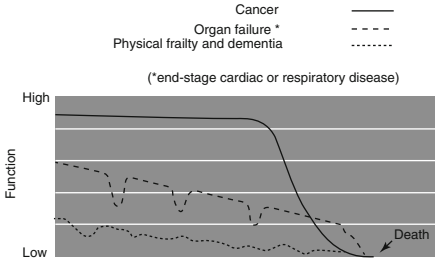
Distinct trajectories of illness over time and towards death are well described in many diseases. Understanding these trajectories can facilitate standard of care and optimal timing of discussions about goals of care, symptom management and advance care planning in the last months of life. A different functional trajectory over the last year of life has been described in CC renal patients (Table 14.3). This is likely to help facilitate best timing and configuration of care.

On average, CC patients report low to moderate levels of physical and psychological symptom distress through the course of their illness. However, they report increasing concerns about the need for information as the duration of illness extends. CC patients also experience a marked increase in symptoms and quite sudden decline in functional status in the last weeks of life. Worsening symptoms may be a much better prognostic indicator than biochemical or other disease markers [11].

However, this 'average' trajectory, which is helpful for service development and planning, does not always reflect the patterns for an individual patient. Amongst CC patients, three discrete symptom trajectories have emerged: (1) relatively stable, (2) steadily increasing and (3) markedly fluctuant, with this pattern occurring more often in those with concurrent cardiac and/or respiratory disease. This latter fluctuant and unpredictable pattern is associated with much higher psychological distress amongst patients and families coping with recurrent acute crises with uncertain outcome. Several investigators have identified that 1–2 weeks prior to death CC patients experience an increase in symptoms. This has been termed the 'tipping point' or transition and is where interventions to address symptoms and other concerns can be targeted to provide most benefit. Further research and a better understanding of illness trajectories in CC and end-stage kidney disease are needed.

Table 14.3 Functional Trajectory Using Karnofsky Performance Scores (KPS) in the last year of life of Conservatively Managed CKD Patients= Left hand side, Recognized Functional Trajectories in various other conditions =Right hand side [11]





Delivering Conservative Care

Once a decision has been made to follow a CC pathway, the emphasis of care should shift from preparation for renal replacement therapy to symptom control, maintenance of residual renal function, avoiding acute medical events likely to destabilise the patient's condition and minimising complications related to CKD. Reversible causes of CKD need to be considered and treated where possible and constant attention paid to minimise pill burden.

Symptom Control

The prevalence and variety of patient reported symptoms is now well recognised. In untreated or newly referred patients, many relate to anaemia and most units are adept at improving and maintaining haemoglobin (Hb) using both iron and subcutaneously administered erythroid-stimulating agents (ESAs) with only occasional need for transfusion. Protocols vary from unit to unit, but in general the availability of erythropoietin and safe intravenous iron preparations have meant that Hb can be maintained at target levels in the majority. In general, target Hb are those used in the dialysis population. Maintenance of Hb has the added advantage of mitigating some of the distress caused by angina and CHF and can improve physical functioning and fatiguability.

Longer-acting ESAs are particularly useful in elderly patients especially if community nurses are required to administer the injections.

Several studies confirm the high prevalence of pain in HD and CKD patients opting for CC. In general NSAIDs are harmful to residual kidney function and may cause or exacerbate GI haemorrhage. Other analgesics, particularly opiates, accumulate or are metabolised differently in advanced CKD [12]. This issue is discussed at length later in this chapter. Hence, caution needs to be exercised to eliminate pain without causing additional problems.

Preserving Residual Function

When supporting residual renal function in elderly CKD patients, clinicians should have several objectives: perhaps the most important is pre-empting and avoiding intercurrent illnesses that can precipitate acute deterioration. In men, care should be taken to consider and treat new or worsening bladder outflow obstruction that might be silently accelerating decline in renal function. Minimising proteinuria and optimising blood pressure and glycaemic control in diabetics are desirable but may not markedly slow progression in this group. In such vulnerable patients, it is often wise to accept trade-offs between optimal control of blood sugar and BP and potential problems created by the tools used to achieve them. Thus, for individual patients the clinician may need to be pragmatic in their interpretation of guidelines

and targets designed for younger and fitter patients. Use of angiotensin-converting enzyme inhibitors (ACEIs) or angiotensin receptor blockers (ARBs) to control both BP and reduce proteinuria is desirable but should be instituted with a close watch on renal function and worsening hyperkalaemia. In practice, if potassium control is difficult, it may be necessary to discontinue them. Discontinuing ACEI or ARBs may have the added benefit of 'buying back' a few mls of residual renal clearance. This strategy has been examined by Goncalves et al. who concluded by questioning the universal pre-emptive initiation of RAS inhibitors in advanced CKD and suggested that they could be safely stopped, at least in some patients particularly those on CC pathways [13]. Caution needs to be exercised, however, if cardio-renal syndrome is present. Whether optimising Hb prolongs residual renal function is not known.

Managing Diet, Nutrition and Fluid Balance

In the era before chronic dialysis became widely available, clinicians advised draconian dietary restrictions to control intake of protein, potassium and phosphate in CKD to extend survival. However, the cost to the patient was often severe malnutrition with profound muscle wasting. In contrast, most CC programmes now emphasise maintenance of a low-salt, normal-protein diet, encouraging patients to eat and enjoy the foods they like, in order to maintain flesh weight and enhance quality of life (QOL). If hyperkalaemia or hyperphosphotaemia becomes problematic, limited dietary restrictions may be appropriate. However, it is important to remain mindful of the important part food contributes towards optimising QOL which underpins the ethos of CC. In reality, elderly and frail CKD patients often lose enjoyment of food as CKD progresses, and renal dieticians need to be creative in augmenting diets rather than restricting them. Food supplements can be used to good effect in some patients.

Controlling phosphate by dietary or pharmacological means may help reduce the distressing symptom of itch. Some authors suggest that optimal Ca and phosphate control slows progression of CKD. However, a balance needs to be established between the potential benefits of phosphate control and the negative effects of dietary restriction and increasing the pill burden in CC patients. Aggressive avoidance or treatment of hyperparathyroidism is only relevant, in this group, if there are symptoms such as bone pain or fractures or as a part of the efforts to alleviate itch. There is some data suggesting that treating hyperparathyroidism, per se, impacts overall survival in CKD patients, but once again the clinician has to judge the relevance of treating a patient with very limited life expectancy. Similarly, many clinicians actively seek to identify and treat reduced vitamin D levels, yet, despite a glut of recent publications concerning ESRD patients, it is not known whether this is advantageous in CC patients.

Finally, many CKD patients erroneously believe that increased fluid intake will 'help' their kidneys to 'work better'. Others have particular difficulty excreting salt

and water because of either concurrent diabetic nephropathy or heart failure. Advice about fluid intake therefore needs to be individualised depending on the particular circumstances pertaining to the patient. Many if not most elderly patients with advanced CKD require diuretics. Loop diuretics are the most commonly prescribed. They can however cause AKI in addition to the existing CKD and exacerbate urinary frequency, nocturia and gout. Consequently, once again, their dose and timing needs to be considered carefully on an individual basis.

Minimising Futile Interventions

If possible, clinicians should clarify, in advance, whether a CC patient wishes to receive dialysis for a limited time to overcome a temporary reduction in renal function that might, for example, result from an intercurrent respiratory tract or other infection. Similarly, 'ceilings of care' in accordance with a patient's wishes may be usefully discussed and documented. Formalised advanced care plans or directives can be helpful and are in general desirable, although uptake of this option where formally offered is low (author's personal experience).

Decision-Making

Decision-making about ESRD is often/always challenging for elderly patients, their families and professionals. There is limited evidence to guide practice. Most people tend to focus on living rather than dying. CKD patients can become accustomed to living with their chronic conditions, and many patients, their families and even their clinicians are reluctant to consider the implications of future deterioration. Others are focussed on their additional co-morbid conditions and can be unaware of the severity and implications of their renal disease. However, based on the small amount of evidence available, important points that elderly patients who choose CC consider in reaching their decision include avoiding poor quality of life, minimising pain and suffering, a desire not to be a burden to care givers, feeling 'too old' for dialysis and that it would be more 'natural' to die without dialysis and not wishing to attend the hospital frequently [14]. Discrete choice experiments in Australian patients suggest that travel restrictions are an important additional consideration and that patients were willing to forgo a surprisingly long duration of life expectancy (23 months, 95 % CI, 19–27) in order to decrease the travel restrictions that dialysis would impose [15]. In general, however, the processes and determinants of decisions for or against the CC are poorly understood. Preserved cognitive function, particularly higher mental function, is clearly an important consideration when appraising patients of treatment options and facilitating informed choice. A proactive and open approach towards decision-making is recommended, but is difficult to achieve. A recent web-based survey of nephrologists in Europe found

that nephrologists decided to offer CC in 5–20 % of patients and a further 5 % of patients chose CC as they refused when nephrologists intended for them to start dialysis [16].

Timely Communication and Advance Care Planning

The importance of timely information, which meets individual patients' preferences, cannot be overstated. Patients with advanced CKD may have been receiving nephrology care for some months or years and become used to living with their renal disease. Thus, it can be difficult for professionals to open up conversations about deterioration or decline in health, and limited survival, when these begin to become relevant. Delivery of optimal palliative and supportive care for patients starts with honest prognostic information, tailored to the patient's information preferences. Many factors prevent good communication, including the inherent uncertainty of prognostication, the uncertainty of an individual trajectory of illness, the imbalance of knowledge between patients and professionals, cognitive impairment and the perceived and actual time limitations in busy health care settings.

The annual mortality rate of dialysis patients approaches 20–24 %. This is higher than that of prostate, breast or colorectal cancer, but many renal patients and their families are not aware of this and consider renal failure as curable with transplantation or treatable with dialysis. Open prognostic information to counter this should be offered even before treatment pathways are considered, but this occurs infrequently.

Advance care planning is a dynamic process that does not occur at one point in time. A good relationship with the patient, and an understanding of their perspectives, is important before having discussions about future priorities and preferences for care. Palliative and supportive care emphasises improving quality of life as end-of-life approaches, and this can only be achieved if there is genuine communication as a foundation for planning, considering outstanding issues and addressing family relationships and conflict. Davison, when studying advanced care planning, showed that patients wanted more information and, in non-medical language on prognosis, disease process and the impact of treatment on daily life [17].

Renal professionals often need prompts to help them open up discussion about the future, as they are much less familiar with how to do this than palliative care professionals. But when sensitive, open exploration of concerns for the future is achieved, the discussion is usually appreciated by patients [18].

Symptom Assessment

Symptom alleviation in renal failure patients is very challenging for many reasons. The symptoms commonly go unrecognised, and renal impairment may constrain management with drugs. It is not always clear whether uraemia or co-morbid

Table 14.4 Symptom assessment scoring systems for renal patients

Edmonton Symptom Assessment System
Memorial Symptom Assessment Scale
The Dialysis Symptom Index
The renal version of the Patient Outcome Scale
The distress thermometer*
Individual symptom scoring systems (pain, depression, pruritus, restless legs syndrome)

*Data only published in abstract form at the time of going to press

conditions are the main cause of each symptom, and for many patients, a combination of factors contributes to their overall symptom burden. The diabetic patient poses particular challenges in this regard and illustrates the difficulties. Diabetic gastroparesis is characterised by anorexia, early satiety, nausea and sometimes vomiting. Advanced uraemia itself also leads to delayed gastric emptying, gastric reflux and dyspepsia. Additional autonomic nerve damage affecting the mid- and lower gut may cause alternating diarrhoea and constipation. Neuropathic pain can be severe, persistent and difficult to control. Skin and soft tissue problems are also common; decubitus ulcers or diabetic foot may occur and amputation may sometimes be required. In these circumstances, clinical judgement skills are critical if complex diagnostic interventions are to be avoided and symptom alleviation maximised which can be helpful (Table 14.4).

A variety of symptom assessment scoring systems have been developed or validated for or used in groups of renal patients. They vary from the long and in-depth memorial symptom assessment score where 32 symptoms are scored for frequency, severity and impact to the simple distress thermometer validated and used widely in cancer services.

Management of Common Symptoms

Pain

Pain is such a common yet under-recognised and under-treated finding in elderly renal patients, and it deserves special attention.

Firstly, removal or specific treatment of the underlying cause of pain is (when feasible) always the best approach, and only when this cannot be achieved should palliation be the main focus. Non-opioid, opioid and adjuvant analgesics can be used in CC patients, but it is critically important not to risk remaining renal function, and careful consideration must be paid to altered metabolism and excretion in the context of renal impairment to avoid unnecessary adverse events.

There are reports of serious side effects following codeine and dihydrocodeine use in patients with advanced renal failure, in particular profound hypotension, respiratory arrest and narcolepsy. For these reasons, they are not recommended.

90 % of tramadol is excreted via the kidneys, resulting in a twofold increase in the elimination half-life in renal impairment; therefore, the dose interval should be increased to twelve hourly, and the dose reduced. Uraemia also lowers the seizure threshold, and tramadol may be more epileptogenic in CC patients.

Morphine and diamorphine are not recommended, because of problems with metabolite accumulation, some of which are clinically active.

Less than 10 % of fentanyl is excreted unchanged in the urine. In renal failure, no dose modification appears necessary. One study however suggests accumulation with sustained administration, and a further study demonstrates reduced clearance. Despite these concerns, fentanyl is, on present limited evidence, one of the preferred opioids in CC patients, and the metabolites are inactive. Some authorities suggest 50 % normal dose if creatinine clearance is <10 ml/min. Careful monitoring for any gradual development of accumulation and toxicity is advised with sustained administration (beyond 1 or 2 days), and there may be some basis for gradual dose reduction if fentanyl is used over days or weeks. Transdermal patches make administration easy. However, a wide individual variation in the pharmacokinetics of fentanyl has been observed and supports a cautious approach.

Alfentanil is shorter acting than fentanyl, but is limited to very end-of-life use as it is only available parenterally.

Buprenorphine because of its high systemic clearance and largely hepatic metabolism has the potential to be reasonably safe in CC patients. Some evidence shows no change in the pharmacokinetics of buprenorphine in renal impairment, but other work shows accumulation of metabolites, although adverse effects have not been reported. Buprenorphine also has the advantage of being available in sublingual, transdermal and injectable preparations (12 Murtagh 2007).

Hydromorphone is likely to accumulate in renal impairment (with proportionately greater accumulation in more severe renal impairment), and clear guidance on its use cannot be given until there is more evidence available.

Methadone is metabolised mostly in the liver and excreted both renally and faecally. There is large interindividual variation and also considerable difference between acute and chronic phase metabolism. Caution should be exercised, and experienced specialist supervision of methadone is required, making it a less valuable tool in CC patients.

Elimination of oxycodone and its metabolites in renal failure is significantly prolonged. There is insufficient evidence to determine whether or not it is safe to use in ESRD patients. Some clinicians use it with caution by reducing the dose and increasing the dosing interval.

Fatigue

Fatigue is multidimensional, with physical, cognitive and emotional elements. Sleep disturbance, poor physical functioning and depression commonly accompanying renal disease may contribute. A number of causes are potentially treatable.

These may be related to the renal disease, e.g. anaemia, or to co-morbid conditions, e.g. hypothyroidism or heart failure, and should be treated aggressively. There is a consistent relationship between haematocrit and energy/fatigue domains in health-related quality of life scores. So for CC patients also, maintenance of Hb is paramount. Non-pharmacological managements of fatigue, such as exercise, cognitive and psychological approaches and complementary treatments, are important, especially as pharmacological interventions become increasingly limited [19].

Nausea and Vomiting

Nausea and vomiting are extremely unpleasant symptoms and are often multifactorial. The first step is to identify any specific cause if present, since cause-directed treatment is most likely to succeed. Uraemia, drugs, gastroparesis or delayed gastric emptying should all be considered. Constipation may exacerbate nausea and vomiting. Poor and/or erratic absorption of oral medications may result, and alternative routes (sublingual, rectal or subcutaneous) need to be considered.

Metoclopramide can be used for delayed gastric emptying or gastroparesis, although doses should be reduced by 50 %, for severe renal impairment. There is also an increased risk of dystonia. Haloperidol or levomepromazine is often used for nausea related to uraemia or drugs, although due to increased cerebral sensitivity, both drugs need dose reduction. 5HT3 antagonists can also be used, although the side effect of constipation needs active management. Because gastritis is common amongst uraemic patients, a low threshold for treatment with a proton pump inhibitor is advised if gastritis is a contributory factor.

Pruritus

The aetiology and pathogenesis of pruritus in ESRD remain unclear, and treatment is frustratingly suboptimal. Current explanatory hypotheses postulate abnormal inflammatory/immune processes, dysfunction in the opioid receptor system and/or neuropathic processes within the nervous system itself.

Thus, immune modulators (such as ultraviolet B light, tacrolimus and thalidomide), opioids antagonists such as naloxone and naltrexone, a relatively new κ-opioid agonist nalfurafine, neuropathic agents (lidocaine, gabapentin) and capsaicin as a counterirritant have all been trialled to treat itch, with varying success. The most commonly used agents, antihistamines, often fail to resolve the itch, but most practitioners would suggest them before moving on to other agents. An important factor in ESRD-related itch is xerosis, or dry skin, that may be a particularly important factor in older people and should be countered with generous and frequent application of emollients. Other common causes of pruritus such as skin disorders; skin infections, e.g. scabies; and liver impairment, especially if the symptom is not resolving, need to be considered.

The first management step is to optimise phosphate levels which contribute significantly to pruritus. Hyperparathyroidism may also be a factor and should be considered. Older people living alone may find it difficult to apply emollients, and spray applications can be helpful in this instance. Preventive measures, such as nail care (keeping nails short), keeping cool (light clothing) and tepid baths or showers are useful concurrent measures. The psychological and social dimensions of severe itch are considerable, and psychological, family and social support is an important component of management [20].

Restless Legs

Restless legs syndrome (RLS) is characterised by uncomfortable sensation and/or an urge to move the legs, worsening at rest, especially during the night. It is often partially or totally relieved by physical activity. The exact cause is not well understood, but the dopaminergic neurons, in the central nervous system, are thought to be disrupted. Iron deficiency, low parathyroid hormone levels, hyperphosphataemia and psychological factors may all play a role. Treatment should involve correction of these factors and reduction of potential exacerbating agents, such as caffeine, alcohol and nicotine. Drugs including sedative antihistamines, metoclopramide, tricyclic antidepressants, selective serotonin uptake inhibitors, lithium, dopamine antagonists and calcium antagonists may also exacerbate RLS.

Much of the evidence for pharmacological treatment in CC is extrapolated from patients with idiopathic restless legs. Gabapentin, dopamine agonists, co-careldopa and clonazepam are the treatments most commonly used, with varying results. All need dose reduction, and gabapentin in particular accumulates rapidly without dialysis and should be used with extreme caution in CC patients [21].

Sleep Disturbance

A detailed history of any sleep disturbance is important, in order to identify sleep apnoea, restless legs syndrome and pruritus, which may be underlying the problem and need treating, in their own right, initially. General sleep hygiene measures are important; avoiding caffeine after lunch, reducing overall caffeine intake, avoiding alcohol (which is both depressant and stimulant) and daytime sleeping. If sleep apnoea is excluded and other exacerbating symptoms treated optimally, and if general measures are unsuccessful, hypnotics may be necessary. Ideally they should be short term, and attempts to re-establish sleep patterns should be made. For those with a longer prognosis, hypnotics carry risk of dependence, and this needs consideration in CC management. The shorter-acting hypnotics, such as zolpidem 5–10 mg, or temazepam 7.5–10 mg are preferable. Longer-acting agents should be avoided as next day overhang sedation may increase the risk of falls.

Breathlessness

The most common causes of breathlessness or dyspnoea in the renal patient are anaemia and pulmonary oedema related to fluid overload or to coexisting cardiovascular or respiratory disease. It is important to identify the cause since treating the cause is almost always the most appropriate and effective first line of management. Once treatment of the underlying cause has been exhausted, then symptomatic measures to relieve breathlessness will be required. These include general and non-pharmacological measures, psychological support and pharmacological measures.

General measures in advanced disease include sitting upright rather than lying (which maximises vital capacity), using a fan or stream of cool air that can provide effective symptom relief, inhaled oxygen if hypoxia is confirmed or suspected and a calm, settled environment. For the patient whose mobility is limited by breathlessness, physiotherapy and occupational therapy can help to maximise mobility and provide appropriate aids to improve function constrained by breathlessness. Since breathlessness is a profoundly unpleasant symptom, assessment and management of the underlying psychological state is important. Breathlessness is very commonly associated with anxiety, often in an escalating cycle (anxiety causing worsening dyspnoea, which triggers worsening anxiety, and so on). Information, education and support of patient and family are therefore critical.

As prognosis worsens, general and non-pharmacological measures will have less to offer, and pharmacological measures directed at the symptom of breathlessness itself may be more appropriate.

Pharmacological treatments directed specifically at breathlessness include low-dose opioids and benzodiazepines (especially if there is moderate or severe associated anxiety). However, there are considerable constraints on the use of opioids in renal patients; the guidance as for pain management should be followed, although dose of opioids for breathlessness is likely to be notably smaller (usually half or quarter the starting dose for pain) and titration upwards is usually not necessary. If small doses are not at least partly effective, combining an opioid such as fentanyl with low-dose midazolam towards the end of life (last few days or hours) may bring relief where either alone is only partially effective. This is often a better strategy than increasing the dose, since adverse effects quickly increase as doses rise.

Benzodiazepines are useful when there is coexisting anxiety but need to be used with care and in reduced doses. Shorter-acting benzodiazepines are recommended, such as lorazepam 0.5 mg orally or sublingually QID (if used sublingually, it has a quicker onset of action and may more readily restore a sense of control to the frightened and anxious patient). If the patient is in the last days of life, midazolam (at 25 % of normal dose if eGFR < 10) can be given subcutaneously and titrated according to effect. Midazolam can be given every 2–4 h, although ESRD patients are sensitive to its effects and do not usually need frequent or large doses. A starting dose of 1.25 or 2.5 mg is often sufficient. If more than one or two doses are required, a subcutaneous infusion over 24 h is most practical. Opiates may have a role as death approaches [22].

Conclusions

People with advanced renal disease who receive CC have extensive need for symptom control, psychological and social support as well as optimal disease management to minimise complications and maintain their residual renal function. They, therefore, need significant medical, nursing, psychological, spiritual and social care particularly as their illness advances towards end of life. High levels of coordination and collaboration between caregivers are paramount. Shared and appropriately informed decision-making backed up by effective and accessible care is recommended.

Key Points

- With increased longevity, advanced stage 5 chronic kidney disease (eGFR < 15 ml/min) has become an increasingly common problem, particularly in frail patients with multiple co-morbidities.
- Current evidence suggests that the survival advantage provided by dialysis is equivocal in patients who are over eighty years with multiple co-morbidities and have poor functional status.
- Initiation of dialysis is often associated with significant cognitive and functional decline in frail elderly patients.
- Over the past decade, a legitimate non-dialytic or conservative care (CC) option has emerged whereby emphasis is shifted towards preservation of residual renal function, symptom identification and management, attention to patient perceived priorities and de-medicalisation of death.
- Limited evidence suggests that quality of life is more favourable and that the number of out-of-hospital and intervention-free days is at least as many in CC patients. They are also less likely to die in acute hospital setting.
- Early and honest discussions about prognosis and patient-centred priorities are advised so that appropriate CC choices can be made and harm avoided.
- A new trajectory of functional decline is seen in CC patients that remains stable until shortly before death when a sharp and short-lived decline is observed.
- When a patient is unable to participate in a dialysis decision and dialysis is not expected to extend life significantly, CC is a reasonable alternative as evidence suggests that dialysis does not alleviate overall symptom burden.

References

1. Thorsteinsdottir B, Montori V, Prokop L, Murad MH (2013) Ageism vs the technical imperative, applying the GRADE framework to the evidence on haemodialysis in very elderly patients. Clin Interv Aging 8:797–807
2. Murtagh FE, Addington-Hall J, Higginson IJ (2007) The prevalence of symptoms in end-stage renal disease: a systematic review. Adv Chronic Kidney Dis 14(1):82–99

3. Jassal SV, Chiu E, Hladunewich M (2009) Loss of independence in patients starting dialysis at over 80 years of age or older. N Engl J Med 361(16):1612–1613
4. O'Connor N, Kmar P (2012) Conservative management of end-stage renal disease without dialysis: a systematic review. J Palliat Med 15(2):228–234
5. Schell J, Da Silva-Gane M, Germain M (2013) Recent insights into life expectancy with and without dialysis, vol 22(2). www.co-nephrolhypertens.com
6. Isaacs A, Burns A, Davenport A (2012) Should maximum conservative management be the standard paradigm for very elderly adults with chronic kidney disease or is there a role for dialysis? J Am Geriatr Soc 60(7):1376–1378
7. Carson RC, Juszczak M, Davenport A, Burns A (2009) Is maximum conservative management an equivalent treatment option to dialysis for elderly patients with significant comorbid disease? Clin J Am Soc Nephrol 4(10):1611–1619
8. Hussain JA, Mooney A, Russon L (2013) Comparison of survival analysis and palliative care involvement in patients aged over 70 years choosing conservative management or renal replacement therapy in advanced chronic kidney disease. Palliat Med 27:829–839
9. Da Silva-Gane M, Welisted D, Greenshields H, Norton S, Chandna SM, Farrington K (2012) Quality of life and survival in patients with advanced kidney failure managed conservatively or by dialysis. Clin J Am Soc Nephrol 7(12):2002–2009
10. Murtagh FE, Marsh JE, Donohoe P, Ekbal NJ, Sheerin NS, Harris FE (2007) Dialysis or not? A comparative survival study of patients over 75 years with chronic kidney disease stage 5. Nephrol Dial Transplant 22(7):1955–1962
11. Murtagh FE, Addington-Hall JM, Higginson IJ (2011) End-stage renal disease: a new trajectory of functional decline in the last year of life. J Am Geriatr Soc 59(2):304–308
12. Murtagh FEM, Chai MO, Donohoe P, Edmonds PM, Higginson IJ (2007) The use of opioid analgesia in end-stage renal disease patients managed without dialysis: recommendations for practice. J Pain Palliat Care Pharmacother 21(2):5–16
13. Goncalves AR, Ahmed AK, El Kossi M, El Nahas M (2011) Stopping rennin-angiotensin system inhibitors in chronic kidney disease: predictors of response. Nephron Clin Pract 119(4):348–354
14. Morton RL, Tong A, Howard K, Snelling P, Webster AC (2010) The views of patients and carers in treatment decision making for chronic kidney disease: systematic review an thematic synthesis of qualitative studies. BMJ 340:c112
15. Morton RL, Snelling P, Webster AC et al (2012) Factors influencing patient choice of dialysis versus conservative care to treat end-stage kidney disease. CMAJ 184(5):E277–E283
16. Van De Luijtgaarden MW, Noordzij M et al (2013) Conservative care in Europe- nephrologists' experience with the decision not to start renal replacement therapy. Nephrol Dial Transplant 28:2604–2612
17. Davison SN, Torgunrud C (2007) The creation of an advance care planning process for patients with ESRD. Am J Kidney Dis 49(1):27–36
18. NHS Kidney Care GMMKC, Advanced Renal Care (ARC) Project (2012) Getting it right: end of life care in advanced kidney disease
19. Lee BO, Lin CC, Chaboyer W, Chiang CL, Hung CC (2007) The fatigue experience of haemodialysis patients in Taiwan. J Clin Nurs 16(2):407–413
20. Keithi-Reddy SR, Patel TV, Armstrong AW, Singh AK (2007) Uremic pruritus. Kidney Int 72(3):373–377
21. Medcalf P, Bhatia KP (2006) Restless legs syndrome. BMJ 333(7566):457–458
22. Jennings AL, Davies AN, Higgins JP, Gibbs JS, Broadley KE (2002) A systematic review of the use of opioids in the management of dyspnoea. Thorax 57(11):939–944