

# Supportive care in advanced chronic kidney disease: Comprehensive conservative care

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## ABSTRACT

Incident and prevalent patients on dialysis are progressively older, with high comorbidity burden and functional dependency. Many could have benefited from a conservative approach, since considerations of symptoms, autonomy, quality of life and hospital-free days are sometimes more important for patients and families than survival. As result, nephrologists around the world are facing challenges to determine which treatment best fits their patients. Comprehensive conservative care in chronic kidney disease care has been recently defined as a holistic, multidisciplinary and patient-centered approach for care of patients with stage 5 CKD. It does not include dialysis, and a shared-decision-making process and advanced care planning are central pillars, providing a way to meet patient and families goals. This review will focus on comprehensive conservative care in CKD in order to provide a communication framework for decision-making process as a guide for nephrologists and other health care professionals.

**Keywords:** Advanced kidney disease, comprehensive conservative care, palliative care

## INTRODUCTION

Chronic kidney Disease (CKD) is an increasing global health problem and is related to the ageing of the population<sup>1-6</sup>. The majority of incident and prevalent dialysis patients are elderly (age  $\geq 65$  years), most of them with significant comorbidities and/or reduced functional capacities. Dialysis may impose an additional symptom burden without bringing improvements in survival or quality of life and with greater health costs<sup>7-10</sup>. Considering this, nephrologists around the world are facing a dilemma to determine which patients are more suitable for conservative treatment as an alternative to dialysis and how to implement and manage it. To assist with that decision, this review will focus and discuss the aspects of comprehensive conservative care in ESRD.

## THE BURDEN OF CHRONIC KIDNEY DISEASE

Advances in health care have contributed to a prolonged life span, with a major increase in chronic medical conditions such as cardiovascular and metabolic diseases. Worldwide, about 60% of deaths are related to chronic conditions and this number is expected to rise by 15% by 2020<sup>1</sup>. CKD already affects about 15% of the world population<sup>2</sup> and has resulted in almost one million deaths worldwide, signifying a rise of 134% between 1990 and 2013<sup>3</sup>. Also, CKD is the 15<sup>th</sup> and 20<sup>th</sup> cause of years lived with disability<sup>4</sup> and disability-adjusted life years<sup>5</sup>. In Portugal, CKD is responsible for 29% of the annual mortality rate (per 100,000 people), with a rise of 84.8% since 1990. It is also responsible

for 782.2 annual years of healthy life lost (per 100,000 people) which have increased by 23.9% since 1990<sup>6</sup>. The costs are extremely high<sup>7</sup>. These results are expected to grow further with the ageing of the population. In fact, older patients are the fastest-growing group of incident ESRD patients and have nearly doubled since 1997<sup>8</sup>. Presently, more than half of patients initiating dialysis are > 60 years of age<sup>9</sup>.

## ■ THE CHALLENGE OF ADVANCED KIDNEY DISEASE CARE

Recent evidence suggests that the overall benefit of dialysis is not the same for all patients<sup>8,9</sup>. For a certain type of patient (advanced age, presence of severe comorbidities or/and poor functional status) the benefit of dialysis in survival is residual and is acquired with a greater time spent in hospital services (including scheduled dialysis treatments), with adverse consequences on quality of life and a greater social burden<sup>10-16</sup>. Those who were managed without dialysis maintained their functional status for longer and with better life satisfaction scores<sup>17</sup>. Additionally, older patients with slower rates of CKD progression can survive a significant amount of time without dialysis<sup>10,13</sup>.

For patients who are already on dialysis, withholding treatment in those with very poor prognosis or in whom dialysis may aggravate clinical condition can be a reasonable option and medical treatment can provide good results<sup>18</sup>. Also, global social and economic crisis have created the need for adequate and just allocation of resources<sup>19</sup>. Portugal has one of the highest rates of incident (226.5 new cases per million) and prevalent (1661.9 cases per million) ESRD patients in Europe and 2.5% of health care costs are attributable to hemodialysis treatments<sup>19</sup>. Considering all this, identifying the ideal patient for conservative treatment and how to approach and manage the care are issues of great debate and priority in nowadays.

## ■ DEFINING CONCEPTS

A range of terms have been used in relation to non-dialytic care in ESRD but without a clear definition. In recent years, there has been an effort to define and organize distinctive concepts (Table 1)<sup>20-22</sup>. The KDIGO 2015 conference on supportive care introduced the concept of “comprehensive conservative care” in the

context of CKD stage 5 not on dialysis, including the interventions to delay progression of kidney disease and minimize risk of adverse events or complications and the palliative care principles and philosophy applied, instead of “renal palliative care” because many health care professionals and patients consider palliative care and terminal care as synonymous, which is not correct<sup>20,22</sup>.

**Table 1**

Definition of concepts in palliative and nondialytic care<sup>20,22</sup>

<b>Palliative Care</b>	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 (WHO definition). It can be provided together with therapies intended to prolong life, including dialysis. Palliative care focuses on the relief of suffering whether the patient is on dialysis or not.
<b>Palliative Dialysis</b>	Approach to dialysis that prioritizes quality of life over survival and seeks the prevention and relief of symptoms and suffering. Interventions are largely to control immediate symptoms and distress while promoting wellbeing and social functioning.
<b>Comprehensive Conservative Care (KDIGO 2015)</b>	Holistic and patient-centered approach for patients with CKD stage 5 <b>not on dialysis</b> that includes interventions to delay progression of kidney disease and minimize risk of adverse events and complications

## ■ COMPREHENSIVE CONSERVATIVE CARE

Comprehensive conservative care for CKD was proposed as a term able to reflect the full extent of conservative management<sup>20</sup>. Three distinct groups were distinguished:

1. Those where conservative care is either chosen or medically advised.
2. Those receiving “choice-restricted” conservative care where resource constraints have prevented or limited access to renal replacement therapy.
3. Those with unrecognized stage 5 CKD, where CKD is present but has not yet been recognized or diagnosed.

Differences in patterns of these groups are seen between lower-middle-income countries, where access

to dialysis may be limited, and high-income countries, where dialysis is more widely available<sup>20</sup>. Further, we will discuss the components of comprehensive conservative care.

### ■ Interventions to delay progression of kidney disease and minimize risk of adverse events and complications

This point regards the management of CKD-related issues according to actual guidelines, including anemia, blood pressure, volume, metabolic disorders, electrolyte and acid-base disorders and CKD-mineral and bone disorders. In Table 2, there are examples of an individualized and patient-centered approach to care for patients with ESRD<sup>23,24</sup>.

The approach is goal direct and prioritizes symptomatic control and avoidance of potential complications that can be manageable in a non-hospital environment. Minimizing the use of drugs and invasive interventions is fundamental. Erythropoiesis-stimulating agents and iron therapy can help to improve weakness, fatigue and dyspnea. Blood pressure control should consider recommended goals but must be adapted to patient age and comorbidities, with attention to deleterious side effects, such as orthostatic hypotension and cognitive decline, particularly in those patients with longstanding hypertension and vascular disease. There is no evidence of benefit of one class of drugs over another in patients who choose conservative care. Volume management helps to ameliorate fatigue and dyspnea, increases quality of life and reduces hospital visits. Limitation of dietary restrictions can improve some nutritional parameters, reduce the risk of hypoglycemia and may contribute to better quality of life. Phosphorus-binding agents, vitamin D analogues and/or calcimimetics to control hyperparathyroidism can reduce pruritus, bone pain and muscle weakness. Similar benefits are seen with correction of metabolic acidosis, generally with sodium bicarbonate, which also helps to improve hyperkalemia. This electrolyte disorder is very prevalent in advanced CKD and may be difficult to manage. Drugs that increase potassium levels may need to be discontinued, optimizing diuretic dosage, and use of cation exchange resins are frequently necessary. When prognosis is poor or the last days are approaching, a symptom management alone to provide comfort may be a choice. Medications that do not meet this goal should be stopped (statins, aspirin, vitamin supplements and others) and medications to treat symptoms should be started as discussed in the next section. Ideally, an expert in palliative care should be involved<sup>20-35</sup>.

**Table 2**

Goal directed approach to patient-centered conservative care in ESRD<sup>23,24</sup>

<b>Anemia</b>	Use ESA* to avoid transfusion and treat symptoms of anemia
<b>Iron deficiency</b>	Treat if suspected related symptoms
<b>Blood Pressure Control</b>	Sufficient to prevent short-term complications (stroke, worsening heart failure)
<b>Volume</b>	Treat to relieve symptoms. Use high-dose diuretics if necessary.
<b>Glycemic control</b>	Sufficient to prevent short-term complications (hypoglycemia, ketoacidosis or hyperosmolar syndrome)
<b>Dyslipidemia control</b>	No intervention is necessary
<b>Nutrition</b>	Reduce dietary restrictions
<b>Electrolyte and acid-base disorders</b>	Treat to avoid symptoms and/or short-term complications
<b>Dysphosphatemia</b>	None intervention unless to control pruritus
<b>Hyperparathyroidism</b>	More permissive, regulate according to related symptoms (generalized bone pain, muscle weakness)
<b>Laboratory monitoring</b>	Minimal necessary
<b>Preventive screening exams</b>	None
<b>Pill burden</b>	For symptom control only

\*ESA – Erythropoiesis Stimulating Agents

### ■ Active symptom management

Advanced CKD is associated with a multiplicity of symptoms which frequently occur in complex clusters, being difficult to treat in isolation<sup>22</sup>. Most are under-recognized, partly because many of them are from comorbid conditions and partly because there is a tendency to focus on biochemical markers and kidney management instead of patient complaints<sup>22</sup>. Most frequent symptoms are fatigue, pruritus and itch, breathlessness/shortness of breath, sleep disorders, restless leg syndrome, depressive symptoms, gastrointestinal symptoms, anorexia and pain. Non-pharmacological approaches should be considered first. Some examples that can improve overall symptoms are cognitive and behavioral therapy, relaxation therapy, aerobic and resistance exercises, sleep hygiene and avoidance of stimulants. Table 3 provides examples of a pharmacological approach to these symptoms.

Geriatric syndromes may be associated with earlier initiation of dialysis therapy (symptoms attributed to uremia) with loss of functional autonomy and increased mortality. The most frequent geriatric syndromes in ESRD are frailty, cognitive impairment, depression, falls and dependency in transfer<sup>25</sup>. Early identification and

**Table 3**

Major symptoms in advanced CKD and pharmacological approaches<sup>20-24</sup>

<b>Fatigue</b>	Treat anemia and iron deficiency. Other modifiable contributing factors that can be treated are vitamin D deficiency, metabolic acidosis, hyperparathyroidism, hypothyroidism, mood disorders; sleep disorders, malnutrition and polypharmacy. Selective serotonin reuptake inhibitors can be used.
<b>Pruritus and Itch</b>	Treat anemia, iron deficiency, hypercalcemia, hyperphosphatemia and xerosis. Exclude drug sensitivities, allergies and contact dermatitis. Topical emollients are first-line therapies (water-based and free from fragrances and additives). Other agents that can be used are topical camphor/menthol, gabapentin or mirtazapine. Antihistamines can help with sleep disturbances. There is some evidence for ondansetron, naloxone and UVB phototherapy.
<b>Breathlessness</b>	Treat anemia, hypervolemia and metabolic acidosis. Encouragement of physical activity in selected cases might help. If anxiety is significant, low-dose and short-acting benzodiazepines such as lorazepam or diazepam may be helpful. Low dose opioids can also be given if carefully monitored to avoid toxicity.
<b>Sleep disorders</b>	Management of secondary causes is fundamental (restless leg syndrome, pruritus, pain, dyspnea, mood disorders, obstructive sleep apnea). Consider low-dose gabapentin post-dialysis, melatonin, zolpidem 5–10 mg nightly, doxepin 10 mg nightly or temazepam 15 mg orally at bedtime
<b>Restless leg syndrome</b>	Treat anemia, iron deficiency, hyperphosphatemia. Avoid medications such as dopamine antagonists, serotonin – norepinephrine reuptake inhibitors, tricyclic antidepressants, calcium channel blockers, opioids.
<b>Depressive symptoms</b>	Address related symptoms like pain, poor sleep and pruritus. Fluoxetine 20–40 mg, sertraline 50–100 mg, paroxetine 10–40 mg, escitalopram 10–20 mg daily can be effective. Tricyclic antidepressants are usually poorly tolerated and abuse of benzodiazepines increases mortality risk.
<b>Gastrointestinal symptoms</b>	Metoclopramide 2.5 mg PO/SC 4/4hours, domperidone orally 10 mg 2–3 times daily if intolerance to metoclopramide, ondansetron 4 mg orally 8/8 hours, haloperidol 0.5 mg PO/SC 4/4 hours, olanzapine 2.5 mg PO 4/4hours. If usual antiemetics are ineffective, levopromazine 6 mg PO/SC once daily may be tried.
<b>Anorexia</b>	Dry mouth (salivix pastilles) and gastroparesia treatment should be first managed. Effective drugs for anorexia are mirtazapine 15–50 mg/day, dronabinol 2.5 mg orally before meals, megestrol 400 mg or prednisolone 10 mg orally per day.
<b>Pain</b>	A step-wise approach to analgesics such as outlined in World Health Organization (WHO) Analgesic Ladder is recommended. Useful adjuvant agents are NSAIDs in refractory musculoskeletal pain, hyoscine butylbromide for colic pain and clonazepam 0.5 mg 12/12h, amitriptyline 10–150 mg, gabapentin 25–300 mg or pregabalin 50–150 mg for neuropathic pain.

optimization of clinical condition is important before a final decision is made about whether or not to start dialysis<sup>25</sup>. Regular symptom assessment using validated tools helps to redirect the treatment. There are eight validated tools to assess global symptom burden in CKD patients, with standouts the Edmonton Symptom Assessment

System-Revised: Renal, the Palliative Care Outcome Scale-Renal and the Dialysis Symptom Index<sup>20</sup>. A meaningful improvement after active symptom treatment has been defined as a 30% improvement in scores<sup>22</sup>.

KDIGO recommends a stepwise approach for symptom management: nonpharmacologic interventions as a first line strategy and then further progress to pharmacologic treatments. Exercise and cognitive behavioral therapy had good results in improvement of sleep disorders, restless leg syndrome, fatigue, pain and depression<sup>22</sup>. Low-dose gabapentin and antidepressants may additionally improve these symptoms<sup>22</sup>. Given the interrelated nature of symptom, an overall symptom approach is like to improve quality of live even if each symptom has not completely resolved. For example, a reduction in pain may improve sleep, humor and ability to cope with disease<sup>22</sup>. Consideration should be given to low-dose therapies that may be effective across several symptoms<sup>20</sup>.

**■ Shared-Decision Making Process**

Following the palliative care principles, KDIGO defines the shared-decision-making process as “a process of communication by which physicians and patients agree on a specific course of action based on a common understanding of the patient’s treatment goals, taking into account the benefits and harms of treatment options and the likelihood of achieving the outcomes that are most important to individual patients”. Because patient’s health status preferences and treatment options may change over time, shared decision making requires a “flexible approach of reevaluation and redirection to ensure that the goals of care and treatment plans remain aligned with patient’s values and preferences”<sup>20</sup>.

Schell et al.<sup>25</sup> has proposed a guide for nephrologists regarding communication and decision making in advanced kidney disease named SPIRES (setup, perceptions and perspectives, invitation, recommendation, empathize, summarize and strategize).

The setup process (preparing for the conversation) is one of the most important stages. It begins with a review of patient’s record for pertinent clinical and laboratory information, followed by the use of prognostic tools to identify patients who may benefit from conservative management.

Prognostic scores can improve accuracy of the prognostic estimates, facilitate informed consent and

support the discussion of supportive care goals<sup>26,27</sup>. In a small study, patients considering dialysis initiation were willing to trade survival time gained in exchange for greater independence and less time in the health care system<sup>27</sup>. Current prognostic tools are not sensitive or specific enough to tell how long the patient will live but are informative at identifying high-risk patients<sup>8,21</sup>. The Renal Physician Association guidelines suggests that patients with 2 or more of the following factors are at high-risk for adverse outcomes with dialysis: age  $\geq 75$  years, a high Charlson Comorbidity index ( $\geq 8$ ), poor functional status or disability (e.g. Karnofsky Performance status  $< 40$ ) and severe malnutrition (serum albumin  $< 2.5$  g/dL).

In recent years, several tools to predict short-term mortality on dialysis and need of kidney supportive care have been developed<sup>8,28-32</sup> and are given in Table 4. Potential new predictors for incorporation in prognostic scores such as potassium, phosphorus, blood pressure, interdialytic weigh gain, SF-36 physical and mental component score and Karnofsky Index are being explored because of their dynamics in the terminal months<sup>8</sup>.

Physician’s clinical experience and judgment may also contribute to identification of high-risk patients. The use of the Surprise Question: “Would I be surprised if this patient died in the next year?” is a validated and easy-to use screening tool. A recent survey of 300 patients with CKD stage 4 to 5 not on dialysis revealed that those who had “no” as an answer died more than 5 times comparatively to those who answer was “yes”<sup>33</sup>. In a study with 150 hemodialysis patients, the answer “no” was associated with a 3.5 times higher mortality than the “yes” group<sup>34</sup>.

An understanding of burdens and benefits of dialysis, considering not just if the patient will survive on dialysis but how the patient will cope with undergoing treatments is also important (Table 5)<sup>25</sup>. After preparing relevant prognostic information, seeking other physicians’ opinions about significant illnesses (heart failure or cancer) can strengthen the information about prognosis and should be encouraged because it helps the nephrologist to understand how likely dialysis is to affect the patient’s overall course<sup>25</sup>. Table 6 summarizes the major principles of the SPIRES approach<sup>25</sup>.

**Table 5**

Potential benefits and burdens of dialysis<sup>23-26</sup>

Potential benefits	Potential burdens
Prolonged life	Dialysis access placement and related complications
Symptom relief	Symptoms related to dialysis itself or its complications
Improved quality of life (ability to remain active and perform activities)	Increased hospitalization rates, time spent in health care system, possible setbacks: acute illness, functional decline and transition to a nursing home
Social aspects of dialysis (support from fellow patients and staff)	Time spent undergoing dialysis or in traveling

■ **Advanced Care Planning**

Early recognition and timely implementation of a management strategy are the mainstems of advanced care planning (ACP). A time-limited trial of dialysis can

**Table 4**

Current validated tools for short-term prognosis assessment of incident dialysis patients<sup>8,21,28-32</sup>

Scores	Population studied	Dialysis Modalities	Mortality Predictors
3-month Survival after dialysis start	–	–	–
US Renal Data System score	28,496 patients (age $\geq 75$ yr)	HD, PD*	Advanced age, low serum albumin, assistance with daily living, nursing home, cancer, heart failure, hospitalization
French REIN Registry score	69,441 patients (age $\geq 67$ yr)	HD, PD*	BMI $<18.5$ Kg/m <sup>2</sup> , congestive heart failure stage III-IV, peripheral vascular disease stage III-IV, behavioral disorder, unplanned dialysis, diabetes, arrhythmia, active malignancy
Catalan Renal Registry score	1365 adult patients with diabetes	HD*	Advanced age, functional dependence, heart disease, central catheter
6-month Survival after dialysis start	–	–	–
US Renal Data System score	28,496 patients (age $\geq 75$ yr)	HD, PD*	Same as for 3-months
French REIN Registry score	4142 patients (age $\geq 75$ yr)	HD, PD*	Advanced age, dementia, peripheral vascular disease III-IV, low serum albumin and the surprise question

\*HD – Hemodialysis; PD – Peritoneal Dialysis



**Table 6**Major principles from SPIRES approach<sup>25,36</sup>

SPIRES	Principles
Setup	Prepare the conversation: review of medical records, application of prognostic tools, individual clinical experience, and other physicians' opinions.
Perceptions and Perspectives	Exploration of patients' knowledge about their disease, hopes, desires and fears. An Ask-Tell-Ask approach (ask before giving information) can be applied for disclosure of prognostic information.
Invitation and Recommendation	Nephrologist's recommendations for the treatment that he thinks to fit best with patients' goals.
Empathize	Anticipation and recognition of adverse emotions. NURSE tool (name the emotion, understand, respect, explore the emotion) is helpful and will allow patients to feel they are heard and cope with information delivered. Avoiding deprivation of hope is fundamental.
Summarize and Strategize	Summarize recommendations and create an advanced care plan that identifies what success looks like (milestones) and setbacks, when dialysis should be reevaluated and/or potentially stopped (pause points).

be applied if there is doubt regarding how the patient may do on dialysis<sup>25</sup>. If there is a positive change in quality of life and health status, it is advantageous to continue with dialysis. However, if it is not, treatment suspension must be considered.

Periodically and scheduled reevaluations are important to reassess if patient's goals are being obtained. Illness trajectories are different from patient to patient. Recently, Xie et al.<sup>37</sup> identified 3 phenotypically distinct functional trajectories in 26,246 patients with CKD stage 4 in a five-year follow-up study: consistent slow decline (trajectory 1), consistent fast decline (trajectory 2) and early nondecline and late fast decline (trajectory 3). Compared with those with consistent slow decline, patients with consistent fast decline had similar risk for kidney outcomes but significantly increased risk of death. Those with early nondecline and late fast decline were at higher risk for death than for kidney disease outcomes.

This highlights the necessity for discussion of possible scenarios in which patients would want to withhold or withdraw dialysis, which are fundamental to avoid potentially unwanted suffering and overuse of limited health care resources<sup>20</sup>. The illness trajectory of declining patients includes sentinel events like acute illness or loss of functional independence that signals the need to reassess care goals<sup>25,35</sup>. These pause points are also opportunities to address burdens that may benefit from

specialized services, such as palliative care for ongoing symptom management<sup>25</sup>.

### ■ Holistic Approach

ACP should be developed using an ethical and holistic approach considering all aspects of patient's life (family, social, cultural and spiritual dimensions) besides medical condition. This implies strict collaboration between nephrologists, palliative care physicians, nutritionists, nurses, and other professionals like social workers, psychologists or priests.

KDIGO recommends that a multidisciplinary team should deliver comprehensive conservative care and the composition of a multiprofessional team should include:<sup>1</sup> nephrologist/nurse/psychosocial worker/counselor or psychologist/dietician/allied health professionals/chaplain;<sup>2</sup> family doctors/community staff/health-care volunteers, and<sup>3</sup> integration and/or liaison with specialist supportive care, according to country and region<sup>20</sup>. Additional efforts are needed to construct these teams and to implement adequate care<sup>20,25,35-39</sup>.

### ■ EVIDENCE REGARDING SURVIVAL IN CONSERVATIVE CARE

Evidence is limited and the range of alternative terms used prevented systematic studies. Also, practically there are no randomized, controlled trials (ethically and practically very difficult) and the remaining studies differ regarding age profile, comorbidity burden, how conservative/dialysis decisions were made, time from which survival is measured, patterns of referral and dialysis management<sup>21</sup>.

The key evidence can be distilled from a group of studies summarized in a systematic review by O'Connor and Kumar<sup>38</sup>. The median survival of those managed conservatively varied from 6 to 23 months. Survival was 65% at 1 year (median 1.95 years) for 75 patients managed conservatively (mainly because of lack of expected survival benefit). After 2 years, 60% had been managed without hospitalizations and the majority (71%) of deaths occurred at home.

A recent five-year prospective observational study compared 122 patients on conservative treatment with 273 patients who attended predialysis clinic (92 of

whom underwent dialysis after an average of 9 months). Patients on conservative management were significantly older, with higher prevalence of dementia, peripheral vascular disease and two or more comorbidities (57% versus 40%,  $p < 0.05$ ) and malnourishment (66% versus 37%,  $p < 0.05$ ). Initial eGFR was similar between groups (MDRD formula). Mean adjusted patient survival was 20 months versus 33 months in the predialysis group ( $p < 0.01$ ). Median survival was 16 months for those managed conservatively and 32% survived more than 12 months after eGFR fell under 10 ml/min per 1.73 m<sup>2</sup>. The major cause of death was the renal disease (62%), followed by cardiac disease (13%) and malignancies (12%). There was no significant difference between all dialysis patients and the group managed conservatively when analysis was restricted to patients aged > 75 years who had two or more comorbidities, at least one of which was congestive heart failure or ischemic heart disease<sup>39</sup>.

Similar findings were found in a large observational study, with no survival benefit for patients > 80 years and for those with lower performance scores<sup>16</sup>.

Chandna et al<sup>40</sup> again reported a survival advantage to dialysis (mean survival of 21.2 versus 67.1 months,  $p < 0.05$ ), with patients managed conservatively being older and sicker. For patients > 75 years, the survival advantage of dialysis reduced to nonsignificant 4 months when corrected for age, high comorbidity and diabetes.

In a group of patients treated with PD, similar findings were also reported. The survival benefit of PD was not observed in those with high burden of comorbidities and functional impairment<sup>41</sup>.

## ■ EVIDENCE ON SYMPTOMS AND QUALITY OF LIFE IN CONSERVATIVE CARE

There is also limited evidence. Systematic review by O'Connor and Kumar<sup>38</sup> again provides good evidence about symptom burden and quality of life. All studies included reported significant symptom burden in those managed conservatively, especially in the last month.

Da Silva-Gane et al.<sup>42</sup> evaluated quality of life every 3 months for up to 3 years in patients with CKD late stage 4 or early stage 5 managed conservatively or by dialysis. Patients on conservative care maintained

quality of life and those who started dialysis, life satisfaction decreased significantly. Only 39% of 3702 nursing home ESRD patients with functional impairment maintained baseline function at 3 months after dialysis initiation, decreasing to 13% at one year<sup>43</sup>.

Brown et al.<sup>39</sup> suggests that renal supportive care can be effective in ameliorating symptoms and maintaining quality of life. Patients treated with dialysis spend more time in hospital and that could have a negative impact on quality of life.

Carson et al<sup>45</sup> showed that every day of additional survival was almost at the expense of a day spent in health care institutions (hospitalization:0.069 versus 0.043 hospital days per patient days survived).

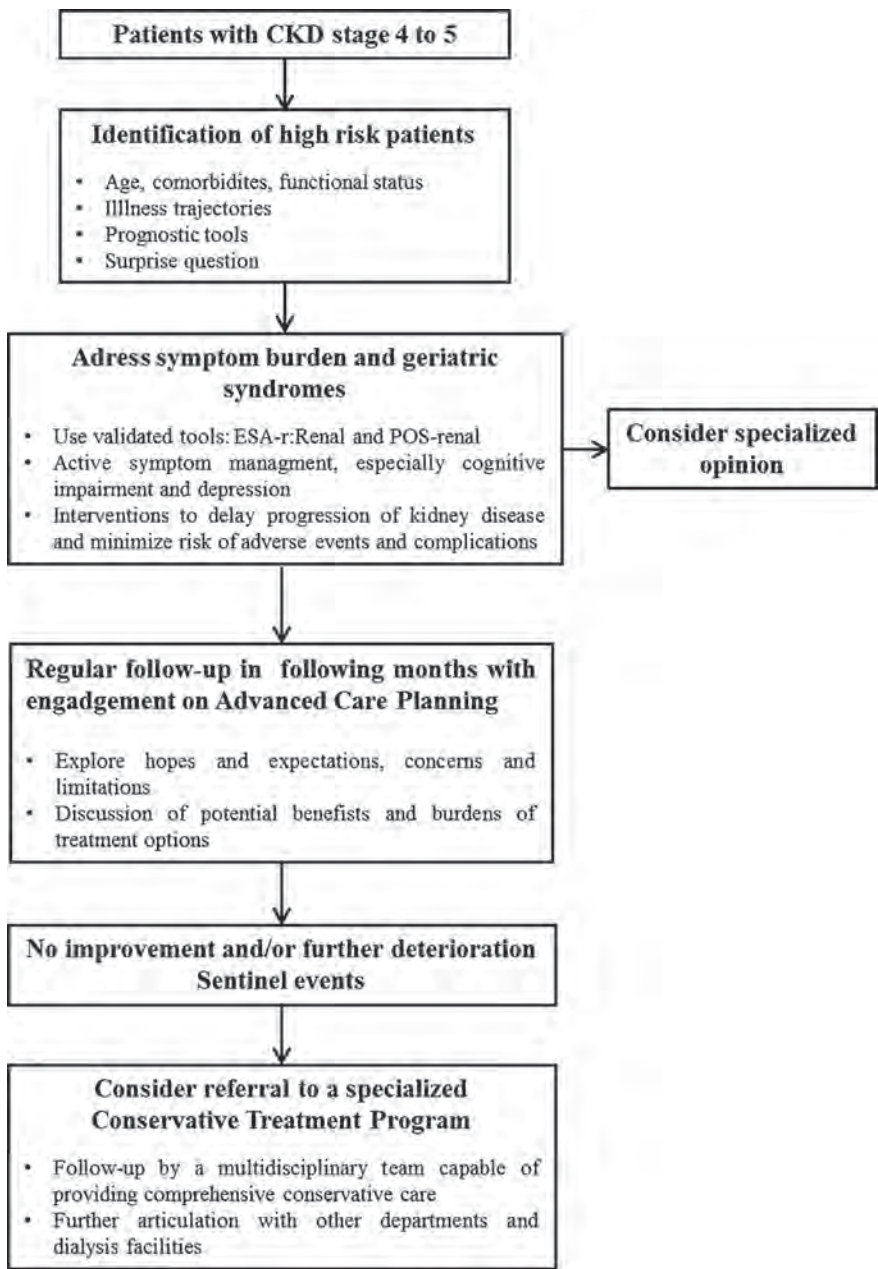
Smith et al.<sup>14</sup> revealed that 65% of deaths among those on dialysis occurred in the hospital compared with 27% of those managed conservatively.

## ■ POLICIES TO PROMOTE CONSERVATIVE AND PALLIATIVE CARE IN ESRD

In Europe, including Portugal, there is an urgent need to strength and develop policies and health care reforms to promote comprehensive conservative and palliative care in ESRD. As an example, a recent survey regarding nephrologists' perceptions about dialysis withdrawal and palliative care in Europe<sup>45</sup> reported that 74% had no specific training in these matters. Tamura et al.<sup>46</sup> identified three major barriers to implementation of a specialized program: access to specific care, capacity to provide it and financial support. The author also suggested five general policies to address these barriers. Universal screening for comprehensive conservative and palliative care needs by nephrologists or other health care providers, with use of validated prognostic and symptom assessment tools previously discussed and documentation of the advanced care plan or surrogate decision maker in the medical record can overcome major access barriers. Training a nephrology workforce to deliver these types of care, along with nurses and other health care providers could be possible through fellowship programs, accreditation organizations and professional societies. Enhancement of conservative and palliative care content and assessment of competencies in nephrology fellowship curriculum would also be important. Monetary funds are fundamental to support the

**Figure 1**

Algorithm proposed by authors for selection and primary management of candidates for ESRD comprehensive conservative treatment



creation of a structured and specialized program with a multidisciplinary team. Implementation of shared-savings model, reimbursement for time-intensive services such as advanced care planning or home-based visits and research collaborations with ESRD multi-institutions could be valuable options<sup>46</sup>.

■ **CONCLUSIONS**

ESRD is becoming an increasingly geriatric condition and the option for a nondialytic management is increasingly recognized and delivered. Comprehensive conservative care has only been recently defined, allowing



a holistic, standardized and stepwise approach for patients who will not do well on dialysis. Evidence suggests that, despite a potentially lower survival, benefits in quality of life and preservation of function outweighs those of dialysis and skills of palliative medicine helps to provide a reasonable symptom control. Patients managed conservatively also consume less health resources which could bring a positive effect in the country's economy. Comprehensive conservative care should be recognized as a core competency and nephrology community should actively support and participate in research to address knowledge gaps and advocate policy changes. The creation of a multidisciplinary team and a specialized medical orientation are major present and future issues in order to optimize outcomes and meet patient's goals. Considering all that was discussed in this article, the authors propose an algorithm (figure 1) that could be applied for selection and primary management of candidates for ESRD comprehensive conservative treatment.

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## References

- Hazzan AD, Halimski C, Agoritsas S, Fishbane S, DeVita MV. Epidemiology and challenges to the management of advanced CKD. *Adv Chronic Kidney Dis* 2016; 23(4): 217-21.
- Hill NH, Fatoba ST, Oke JL, Hirst JA, O'Callaghan CA, Lasserson DS, et al. Global prevalence of Chronic Kidney Disease – a Systematic Review and Meta-Analysis. *PLoS One*. 2016 Jul 6;11(7):e0158765.
- GBD 2013 Mortality and Causes of Death Collaborators. Global, regional, and national age–sex specific all-cause and cause-specific mortality for 240 causes of death, 1990–2013: a systematic analysis for the Global Burden of Disease Study 2013. *Lancet* 2015; 385: 117-71.
- Global Burden of Disease Study 2013 Collaborators. Global, regional, and national incidence, prevalence, and years lived with disability for 301 acute and chronic diseases and injuries in 188 countries, 1990–2013: a systematic analysis for the Global Burden of Disease Study 2013. *Lancet* 2015; 386: 743-800.
- Murray CJL, Barber RM, Foreman KJ, et al. Global, regional, and national disability-adjusted life years (DALYs) for 306 diseases and injuries and healthy life expectancy (HALE) for 188 countries, 1990–2013: quantifying the epidemiological transition. *Lancet* 2015; 386: 2145-91.
- <http://global-disease-burden.healthgrove.com/l/67121/Chronic-Kidney-Disease-in-Portugal>. [Accessed 19 April, 2017]
- Morton RL, Tamura MK, Coast J, Davison SN. Supportive care: economic considerations in advanced kidney disease. *Clin J Am Soc Nephrol* 2016; 11(10): 1915-20.
- Couchoud C, Hemmelgarn B, Kotanko P, Germain MJ, Moranne O, Davidson S. Supportive care: time to change our prognostic tools and their use in CKD. *Clin J Soc Nephrol* 2016; 11(10):1892-1901;
- Cohen LM, Ruthazer R, Moss AH, Germain MJ. Predicting six-month mortality for patients who are on maintenance hemodialysis. *Clin J Am Soc Nephrol* 2010; 5(1): 72-9.
- Berger JR, Hedayati SS. When a conservative approach to advanced chronic kidney disease is preferable to renal replacement therapy? *Seminars in Dialysis* 2015; 27(3): 253-6.
- Noordzij M, Jager K. Increased mortality early after dialysis initiation: a universal phenomenon. *Kidney Int* 2014; 85(1): 12-4.
- Bradbury BD, Fissel RB, Albert JM, et al. Predictors of early mortality among incident US hemodialysis patients in the Dialysis Outcomes and Practice Patterns Study (DOPPS). *Clin J Am Soc Nephrol* 2007; 2: 89-99.
- Murtagh FEM, Marsh JE, Donohoe P, Ekbal NJ, Sheerin NS, Harris FE. Dialysis or not? A comparative survival study of patients over 75 years with chronic kidney disease stage 5. *Nephrol Dial Transplant* 2007; 22: 1955-62.
- Smith C, Da Silva Gane M, Chandna S, Warwicker P, Greenwood R, Farrington K. Choosing not to dialyze: evaluation of planned non-dialytic management in a cohort of patients with end-stage renal failure. *Nephron Clin Pract* 2003; 95: c40-6.
- Carson RC, Juszcak M, Davenport A, Burns A. Is maximum conservative management an equivalent treatment option to dialysis for elderly patients with significant comorbid disease? *Clin J Am Soc Nephrol* 2009; 4: 1611-9.
- Hussain JA, Mooney A, Russon L. Comparison of survival analysis and palliative care involvement in patients over 70 years choosing conservative management or renal replacement therapy in advanced chronic kidney disease. *Palliat Med* 2013; 27(9): 829-39.
- Tamura MK, Covinsky KE, Chertow GM, Yaffe K, Landefeld S, McCulloch CE. Functional status of elderly adults before and after initiation of dialysis. *N Engl J Med* 2009; 361(16): 1539-47.
- Germain MJ, Davison SN, Moss AH. When enough is enough: the nephrologist's responsibility in ordering dialysis treatments. *Am J Kidney Dis* 2011; 58(1): 135.
- Coelho A, Diniz A, Hartz Z, Dussault G. Gestão integrada da doença renal crónica: análise de uma política inovadora em Portugal. *Ver Port Saúde Pública* 2014; 32(1): 69-79.
- Davison SN, Levin A, Moss AH, Jha V, Brown EA, Brenann F, et al. Executive Summary of the KDIGO Controversies Conference on Supportive Care in Chronic Kidney Disease: developing a roadmap to improving quality care. *Kidney Int* 2015; 88(3): 447-59.
- Murtagh FEM, Burns A, Moranne O, Morton RL, Naicker S. Supportive care: comprehensive conservative care in end-stage kidney disease. *Clin J Am Soc Nephrol* 2016; 11(10): 1909-14.
- Davison SN, Jassal SV. Supportive care: integration of patient-centered kidney care to manage symptoms and geriatric syndromes. *Clin J Am Soc Nephrol* 2016; 11(10): 1882-91.
- Vandecasteele SJ, Tamura MK. A patient-centered vision of care for ESRD: dialysis as a bridging treatment or as a final destination? *J Am Soc Nephrol* 2014; 25: 1647-51.
- Grubbs V, Moss AH, Cohen LM, Fischer MJ, Germain MJ, Jassal V, et al. A palliative approach to dialysis care: a patient centered transition to the end of life. *Clin J Am Soc Nephrol* 2014; 9(12): 2203-9.
- Schell JO, Cohen RA. A communication framework for dialysis decision-making for frail elderly patients. *Clin J Am Soc Nephrol* 2014; 9: 2014-21.
- Renal Physicians Association. Shared Decision-Making in the Appropriate Initiation of and Withdrawal from Dialysis. 2nd ed. Rockville, MD: Renal Physicians Association; 2010.
- Davison SN. End-of-life care preferences and needs: perceptions of patients with chronic kidney disease. *Clin J Am Soc Nephrol* 2010; 5: 195-204.
- Thamer M, Kaufman JS, Zhang Y, Zhang Q, Cotter DJ, Bang H, et al. Predicting early death among elderly dialysis patients: Development and validation of a risk score to assist shared decision making for dialysis initiation. *Am J Kidney Dis* 2015; 66: 1024-32.
- Couchoud CG, Beuscart JB, Aldigier JC, Brunet PJ, Moranne OP. REIN Registry: Development of a risk stratification algorithm to improve patient-centered care and decision making for incident elderly with end-stage renal disease. *Kidney Int* 2015; 88: 1178-86.
- Couchoud C, Labeeuw M, Moranne O, Allo V, Esnault V, Frimat L, et al. French Renal Epidemiology and Information Network (REIN) registry: A clinical score to predict 6-month prognosis in elderly patients starting dialysis for end-stage renal disease. *Nephrol Dial Transplant* 2009; 24: 1553-61.
- Mauri JM, Vela E, Clèries M. Development of a predictive model for early death in diabetic patients entering hemodialysis: A population-based study. *Acta Diabetol* 2008; 45: 203-9.
- Cohen LM, Ruthazer R, Moss AH, Germain MJ. Predicting six-month mortality for patients who are on maintenance hemodialysis. *Clin J Am Soc Nephrol* 2010; 5: 72-9.
- Javier AD, Figueroa R, Siew ED, Salat H, Morse J, Stewart TG, et al. Reliability and utility of the surprise question in CKD stages 4 to 5. *Am J Kidney Dis* 2017; pii: S0272-6386(17)30006-9
- Moss AH, Ganjoo J, Sharma S, Gansor J, Senft S, Weaner B, et al. Utility of the "surprise" question to identify patients with high mortality. *Clin J Am Soc Nephrol* 2008; 3: 1379-84.
- Koncicki HM, Schell JO. Communication skills and decision making for elderly patients with advanced kidney disease: a guide for nephrologists. *Am J Kidney Dis* 2016; 67(4): 688-95.
- Davison SN, Torgunrud C. The creation of an advanced care planning process for patients with ESRD. *Am J Kidney Dis* 2007; 49(1): 27-36.
- Xie Y, Bowe B, Xian H, Balasubramanian S, Al-Aly Z. Estimated GFR trajectories of people entering CKD stage 4 and subsequent kidney disease outcomes and mortality. *Am J Kidney Dis* 2016; 68(2): 219-28.
- O'Connor NR, Kumar P. Conservative management of end-stage renal disease without dialysis: a systematic review. *J Palliat Med* 2012; 15: 228-35.
- Brown MA, Collet GK, Josland EA, Foote C, Li Q, Brennan FP. CKD in elderly patients managed without dialysis: survival, symptoms and quality of life. *Clin J Am Soc Nephrol* 2015; 10: 260-8.
- Chandna SM, Da Silva-Gane M, Marshall C, Warwicker P, Greenwood RN, Farrington K. Survival of elderly patients with stage 5 CKD: comparison of conservative management and renal replacement therapy. *Nephrol Dial Transplant* 2011; 26: 1608-14.
- Shum CK, Tam KF, Chak WL, Chan TC, Mak YF, Chau KF. Outcomes in older adults with stage 5 chronic kidney disease: comparison of peritoneal dialysis and conservative management. *J Gerontol A Biol Sci Med Sci* 2014; 69: 308-14.
- Da Silva-Gane M, Wellsted D, Greenshields H, Norton S, Chandna SM, Farrington K. Quality of life and survival in patients with advanced kidney failure managed conservatively or by dialysis. *Clin J Am Soc Nephrol* 2012; 7: 2002-9.

43. Kurella TM, Covinsky KE, Chertow GM, Yaffe K, Landefeld CS, McCulloch CE. Functional status of elderly adults before and after initiation of dialysis. *N Engl J Med* 2009; 361:1539-47.
44. Carson RC, Juszczak M, Davenport A, Burns A. Is maximum conservative management an equivalent treatment option to dialysis for elderly patients with significant comorbid disease? *Clin J Am Soc Nephrol* 2009; 4: 1611-19.
45. Biesen WW, Lujtgaarden WM, Brown EA, Michel JP, Munster BC, Jager KJ, et al. Nephrologists' perceptions regarding dialysis withdrawal and palliative care in Europe: lessons from a European Renal Best Practice survey. *Nephrol Dial Transplant* 2015; 30(12): 1951-58.
46. Meier DE, Tamura MK. Five policies to promote palliative care for patients with ESRD. *Clin J Am Soc Nephrol* 2013; 8: 1783-90.

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