

Review

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Palliative Care for Nephropathic Patients

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ABSTRACT

A new light has recently been shed on palliative care, especially, on its multidisciplinary approach developed to improve the Quality of life of seriously ill patients and their families. However, palliative care is still often mistakenly referred to as an end-of-life care and wrongly interchanged with hospice care. Nephropathic patients usually present a decrease in expectancy and Quality of life and may benefit from palliative care as opposed to hospice care. Palliative care requires a tight collaboration among different health care professionals, patients and their families, to share diagnosis, prognosis, realistic goals of treatment and therapeutic decisions. Several approaches may be attempted to improve the Quality of life of chronic nephropathic patients, such as palliative dialysis, conservative management and peritoneal dialysis. For example, personalized goals and a wider concept of adequacy of extracorporeal treatment are the bases of palliative dialysis. In specific subgroups of frail patients, the pharmacological conservative management could be more appropriate than extracorporeal treatment, as the former reduces the burdens derived from invasive procedures. Finally, peritoneal dialysis could be an important option for frail patients to avoid an aggressive extracorporeal treatment while maintaining a gentle solute and fluid control. However, only limited evidences are available on palliative and hospice care performed on patients with Acute Kidney Injury (AKI). Herein, the main variables affecting the medical decision-making on palliative care in nephropathic patients are described, and the different approaches available to improve quality of palliative care during Chronic and Acute Kidney Injury are analyzed.

KEYWORDS: Palliative care; Hospice care; Chronic Kidney Disease; End-Stage Renal Disease; Acute Kidney Injury; Renal Replacement Therapy

ABBREVIATIONS: AKI: Acute kidney Injury; CKD: Chronic Kidney Disease; ESRD: End-Stage Renal Disease; RRT: Renal Replacement Therapy; ERA-EDTA: European Renal Association-European Dialysis and Transplant Association; MCM: Maximum Conservative Management; PD: Peritoneal Dialysis; ICU: Intensive Care Unit

INTRODUCTION

Palliative care has recently been reconsidered as a multidisciplinary approach to care which has been developed to support clinicians in the management of patients with serious

illness.¹ This innovative perspective is aimed to improve the Quality of life of patients and their families through a multidimensional analysis involving: 1) identification and management of patients' physical, psychological and spiritual symptoms; 2) evaluation of patients' clinical condition and prognosis to establish realistic and appropriate treatment goals; 3) arrangement of individualized therapeutic plans according to patients' wishes; 4) attention to families' needs and 5) support for health care providers.¹

Currently, the specialty palliative care is mainly offered in patients within hospices or hospitals only when life-prolonging treatment has failed;² as a consequence, most of health care professionals perceive palliative care as a synonymous of End-of-life care.² However, limiting palliative care only to these situations may exclude the majority of serious conditions, such as advanced cancer or end-stage organ dysfunction, which severely affect patients' physical and psychological symptoms.^{2,3} For these reasons, palliative care should be provided together with life-sustaining treatments and considered as an integral component of comprehensive therapy for critical and non-critical care patients. Therefore, palliative care is neither a mutually exclusive alternative to intensive care, nor a sequel to failed attempts with life-prolonging care,¹ in fact, according to the definition developed by the Center to Advance Palliative Care and the American Cancer Society, "Palliative care is appropriate at any age, at any stage in a serious illness, and can be provided together with curative treatment".² On the other hand, hospice care is strongly recommended for patients who have a physician-estimated life expectancy of 6 months or less and who are undergoing restorative treatments and foregoing curative therapy.²

Despite the improvements in therapeutic options, patients with AKI as well as those with Chronic Kidney Disease (CKD), especially those with End-Stage Renal Disease (ESRD), have a shorter life expectancy compared to patients without nephropathies. Extracorporeal replacement therapies may increase survival rates of these patients; however, for a specific subgroup of acute critically ill patients, these procedures are often unable to improve outcomes and prolong the physiological process of death, worsening the quality of the End-of-life stage of these patients.

Several clinical trials have shown the benefits derived from the early application of palliative care in subgroups of seriously ill patients, such as those with advanced cancer,⁴ multiple sclerosis⁵ or congestive heart failure.^{6,7} However, the provision of palliative care to nephropathic patients with CKD or AKI is heterogeneous across different countries and often mistakenly identified with hospice care. Currently, the use of palliative care in the nephropathic population is inadequate; it is recognized in the UK, USA, Italy and Canada mainly for ESRD patients⁸⁻¹² and is usually limited to the last phase of life. Finally, an adequate approach for palliative care is still largely lacking for patients with AKI.

The aim of this review is to describe the main variables affecting the medical decision-making on palliative care in nephropathic patients and to analyze the different approaches to improve quality of palliative care during Chronic and Acute Kidney Injury.

PALLIATIVE CARE FOR CKD PATIENTS

Demand for dialysis is constantly increasing all over the world, especially in the elderly population.^{13,14} As clearly demonstrated by the European Renal Association-European Dialysis and Transplant Association (ERA-EDTA), the European incidence of ESRD requiring dialysis procedures among patients aged > 65 years increased from 22% in 1980 to 55% in 2005.¹⁵ The recent technological advancements observed with the Renal Replacement Therapy (RRT) have increased feasibility of these techniques and have improved survival for a large number of patients with ESRD.

Despite the increased survival, an annual mortality rate of about 23% has been reported for ESRD patients undergoing RRT¹⁶ which mainly depended on the high prevalence of other chronic comorbidities, such as diabetes, hypertension and cardiovascular diseases.¹⁷ A reduction in the overall functional status during the first 12 months after initiation of RRT has been reported for patients with CKD and, specifically, for a subgroup of nursing home residents.¹⁸ Finally, an increasing burden of somatic and psychological symptoms as well as a worsening of social conditions have been often observed among ESRD patients undergoing RRT.¹⁹ These symptoms, whose prevalence is comparable to those observed in cancer patients,²⁰ severely affect the patient's Quality of life.¹⁹ In these conditions, a high proportion of elderly patients regrets the decision to start dialysis and thus, after agreeing with caregivers, prefers a conservative management for ESRD.²¹

Training, information and support for patients, their family and caregivers are pivotal for planning the management of care of ESRD patients. In particular, other therapeutic options such as, extracorporeal treatment, Peritoneal Dialysis (PD) or Conservative therapy should be discussed and comprehensively shared among patients, family and health care providers. Both for patients undergoing RRT and for those managed with conservative therapy, palliative medicine should be taken into consideration in order to improve the Quality of life.

EXTRACORPOREAL RRT

Extracorporeal therapy is the most utilized treatment to replace renal function in ESRD patients.²² Adequacy of extracorporeal treatment is often identified with the concept of solute clearance, which is usually quantified through Kt/V measurement. However, the strong effort in treatment personalization has recently encouraged to carefully evaluating the specific target of therapy, which has to aim not only at the solute removal

but rather at the improvement of the whole patient's clinical picture. Although reasonable and attractive, this concept is still far from being applied in most dialysis centers in the daily clinical practice.

Indeed, following analysis of data on treatment targets in CKD patients from 12 countries, the Dialysis Outcomes and Practice Patterns Study (DOPPS) showed no difference in dialysis prescription across subgroups of patients with different clinical requirements. For instance, the same treatment time, normalized by body weight, was prescribed both for patients aged < 45 years and frail elderly patients.²³ Targeting the normalization of dry weight, Kt/V and serum phosphorus, may not be the primary treatment objective for all patients.¹⁵ Apart from these specific clinical issues, the concept of adequacy of RRT should also take into account the ability to achieve other treatment goals, such as the improvement of the Quality of life of patients and their families, the prevention and relief from suffering, the identification and treatment of pain and other physical and psychosocial conditions.

In a recent paper, Romano and Palomba proposed the concept of palliative dialysis as a change in perspective for the treatment goals achievable by using either ultrafiltration or dialysis alone, depending on the clinical objectives.¹⁵ In this scenario, an individualized RRT prescription overlaps with the requirement of palliative care and it may improve the physical, emotive and autonomy-related issues (Figure 1).

As such, the delivery of palliative care should be started not during the last moments of patients' lives but, concomitantly with RRT.¹⁵

The quality of care given to the patients may be eval-

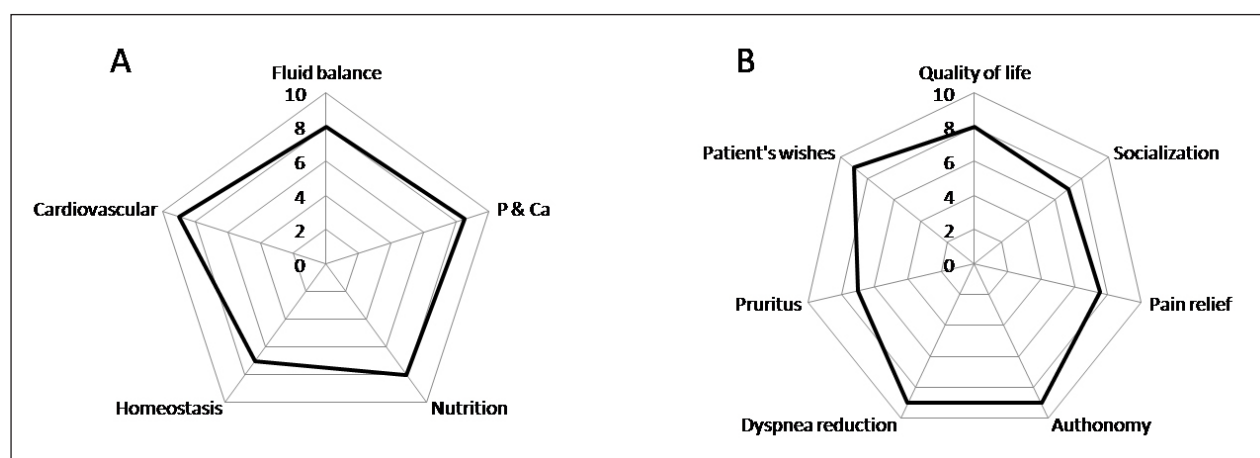
uated through the PEACE score: a simple tool addressing six domains on physical, emotive, autonomy-related symptoms; communication and completion of life issues; economic burden and religious beliefs.²⁴ However, although this tool may be of help for clinicians, the most important factor to consider when making a clinical decision is the autonomy of the patient who faces ESRD and of the relatives who provide support.¹⁵ In particular, Parlevliet et al. showed that caregivers are often forced to change their routine and professional schedules, and 84% of them feel overburdened by the situation.²⁰

Among the most frequent symptoms observed in ESRD patients, such as lack of energy, drowsiness, dry mouth, pain, sleep disturbance, restless legs, pruritus, dry skin and constipation,²⁵ dyspnea may be the most manageable with palliative dialysis.¹⁵ Indeed, although other symptoms can be treated with medications, fluid overload and acidosis are rarely controlled in ESRD patients conservatively managed.¹⁵

CONSERVATIVE MANAGEMENT

Conservative management should be taken into account for patients who are not eligible for extracorporeal treatment or who refuse it. It is based on a pharmacological and behavioral approach used to prevent the major complications of ESRD, such as hydro-electrolytic unbalance, acid-base disorders, hyperazotemia and anemia. This option is usually limited to patients with severe comorbidities and geriatric conditions, such as dementia and frailty.¹⁵

Frailty, in particular, is a multidimensional construct reflecting the decline in health and organ function observed in elderly; it occurs in approximately 67% of dialysis patients.²⁶ Frailty is correlated with an increased risk for disability, hospi-



Graph of a chronic extracorporeal renal substitution for CKD patient (panel A) and graph of palliative dialysis for "CKD end-of-life" patient (panel B). Each graph takes into consideration several variables differently affected by the treatments (0: the variable is minimally influenced; 10: the variable is strongly improved).

The adequacy of the treatment may be identified by the area within the graph: during an ideal therapy, the inner area covers 100% of the graph. For a treatment to be "adequate", other parameters than solute clearance or fluid balances should be considered for end of life patients; in this scenario, an individualized RRT prescription should improve the physical, emotive and autonomy-related issues.

Figure 1: "Adequacy" of Extracorporeal treatment and the role of Palliative dialysis.

talization, institutionalization and death²⁷ and it is clinically diagnosable through recognition of unintentional weight loss, slow walking speed, weakness, exhaustion and low level of physical activity.²⁸ The use of conservative management is recommended in patients with this clinical picture.

In line with this view, Maximum Conservative Management (MCM) is a European proposal based on a multidisciplinary approach with nutritionists, social workers, psychologists and other health professionals aimed at improving the Quality of life of frailty patients with ESRD.²⁹ Despite patients who received RRT showed a higher survival rate than those who received MCM, they had higher rates of hospitalization and in-hospital death.³⁰

Although necessitating the lowest institutionalization requirement, the conservative management requires close monitoring and treatment adjustment by several professional figures in order to avoid treatment failure. In particular, a constant sharing of achievable therapeutic goals should be encouraged between general practitioners or specialists on one side and patients and their families on the other. This procedure aims to reduce accesses in emergency department and thus invasive procedures and hospitalizations. Nevertheless, a multidisciplinary approach is required to limit patient's symptoms and suffering from a home delivery palliative care system.

PERITONEAL DIALYSIS

Another type of management available is Peritoneal Dialysis (PD); its use is suggested in frail patients as, in this specific subgroup of nephropathic patients, PD may offer advantages with respect to both extracorporeal RRT and conservative management. Indeed, hemodynamic instability and severe hypotension may affect extracorporeal RRT, further worsening frail patients' clinical conditions. PD is considered a less invasive treatment, which guarantees a slow, continuous dialysis and ultra filtration; it is usually more tolerated by patients and it may preserve better renal function, hence allowing a less restricted and more patient-friendly diet. As well as extracorporeal RRT, PD is able to compensate metabolic acidosis and fluid overload that may cause exacerbation of patients' condition in conservative management. However, similarly to conservative therapy, PD may be managed through home care and occasionally scheduled ambulatory visits, making it an effective choice for patients requiring palliative or hospice care.³¹

In 2008 ERA-EDTA pointed out some criteria that may be used to recommend PD.³² In particular, clinical conditions that may be usually identified in frail patients, such as aging complications, severe Cardiac Disease or Peripheral Vascular Disease, have been recognized as potential indicators for PD prescription. However, ERA-EDTA also identified factors with which use of PD may be contraindicated; these factors include inadequate patient's physical ability and lack of familiar or social support. In fact, the family involvement in the patient's disease is more

demanding in PD than in extracorporeal RRT and conservative management, considering that a technical training of the patient and/or caregiver to the peritoneal dialytic procedure is mandatory.

Despite a close cooperation between patients, their families, general practitioner, nurses and nephrologists is required, PD may guarantee a better quality of life, becoming thus the therapy of choice in a selected population requiring palliative or hospice care.

PALLIATIVE CARE FOR AKI PATIENTS

AKI frequently occurs in critically ill patients in the Intensive Care Unit (ICU), with an estimated global prevalence of 36%-67%;³³ it exhibits different etiologies and several pathophysiological mechanisms, and is correlated with a high mortality rate.³⁴⁻³⁸

Despite the poor prognosis associated with AKI, the concepts of palliative and hospice care are still underdeveloped for this specific subgroup of patients. Indeed, despite a growing interest in the literature on palliative care for critically ill patients in the ICU, only few papers have been focused on the withdrawal or withholding of invasive treatments in acute nephropathic patients. In particular, a systematic search of the published literature, performed on Pub Med using the following key words "Acute Kidney Injury" AND ("Palliative care" OR "Palliative medicine") and related MeSH terms, revealed 87 citations. Among them, 10 are specifically focused on "acute-on-chronic" conditions and advanced planning for ESRD patients; 32 couple AKI with other life-threatening conditions (e.g. heart failure or cancer) and underline the importance of palliative care medicine in these diseases; 39 are not relevant for this particular topic. Only 11 papers are specifically focused on palliative care for nephropathic patients with AKI. Among these, 5 reviews the ethical issues.³⁹⁻⁴³ and 3 specifically describe the epidemiology and clinical factors associated with End-of-life in AKI patients.⁴⁴⁻⁴⁶

For these reasons, while palliative and hospice care management is globally applied in CKD patients, even general indications are still lacking in AKI patients. Nowadays, clinicians are often faced with critically ill patients who meet the criteria for initiating RRT, however, there are uncertainties on whether the patient would likely benefit from these procedures.⁴⁷ In fact, although critically ill patients are often subjected to advanced and invasive diagnostic and therapeutic interventions, mortality in the ICU remains very high.⁴⁸ Therefore, in these settings, advanced life support procedures and systems, such as RRT, may only unreasonably postpone the time of death.⁴⁹

Scarce literature is available to guide clinicians in the decision to discontinue RRT in patients who will no longer benefit.⁴⁷ Although an evidence-based guideline on this use has been already produced by the Renal Physicians Association and the American Society of Nephrology,⁴² only a small number

of nephrologists and intensivists are aware of it.¹¹ As a consequence, clinical practice on withholding or withdrawal of RRT is variable and based primarily on the local institutional practice, physicians' clinical judgment, available resources and local management.^{36,38,50-52}

Several factors should be taken into consideration during the decision-making process regarding the withholding or withdrawal of RRT in patients with AKI, including feasibility, survival prediction, renal functional recovery prediction and quality of life.

Clinical *feasibility* is certainly an important limiting factor. Although several patients' clinical conditions (e.g., severe hypotension) might negatively affect the technical feasibility, new techniques such as continuous Renal Replacement Therapies have allowed performing RRT in the vast majority of patients.⁴⁷

An adequate medical judgment and an informed patient and family consent cannot ignore *survival prediction* as an important factor to be considered when deciding to continue, withhold or withdraw RRT. Despite several organ dysfunction scoring systems⁵³ and outcome prediction models available to help clinicians identify severely ill patients, none of them actually provide physicians with enough information on the suitability of intensive care treatments for the individual patient.⁴⁹ Short and long term mortality of critically ill patients who developed AKI and required RRT is globally high (46-75%).⁵⁴ The Study to Understand Prognoses and Preferences for Outcomes and Risks of Treatments (SUPPORT), the largest prospective study investigating survival in critically ill patients, has shown that the mean survival time in patients who required dialysis was of approximately 30 days and that only 27% of patients were alive after 5 months.⁵⁵

Prediction of renal functional recovery after AKI should be considered as another important factor in determining long-term renal and non-renal outcomes⁵⁶⁻⁵⁹ in the decision-making process.⁴⁷

The *Quality of life* of patients and their families may be severely affected if ESRD occurs and chronic extracorporeal RRT is required after an episode of AKI. However, long-term outcomes and Quality of Life of critically ill patients requiring RRT have been examined only in few studies.⁴⁷ For instance, in the SUPPORT study, AKI patients who survived to the critically ill stage showed a median of one dependence in activities of daily living;⁵⁵ however, different results are shown in the published literature.^{43,60,61}

Unlike in CKD patients, in critically ill AKI patients the time frame window to discuss the decision to initiate or stop RRT is often unavailable. Therefore, not knowing the *patient's own wishes* make the clinical judgment even harder,⁶² and hence

pressure to make a decision builds up among family and the health care team.⁴⁷

According to the Renal Physicians Association/American Society of Nephrology guidelines of shared decision making in dialysis, a time-limited trial of RRT could be considered for patients with uncertain prognosis.⁶³ In particular, it may result useful when a disagreement in management occurs between physicians and nurses or patients' families.⁴⁷ End-points, goals and duration of this time-limited trial should be exactly defined in advance. In particular, specific criteria, their magnitude of change accepted as evidence for improvement and the time point of their evaluation should be established and agreed between physicians, nurses, patients and their families.⁴⁷ Notably, the decision making regarding the withholding or withdrawal of RRT in patients with AKI during a time-limited trial is an ongoing process: clinical outcomes as well as patients' prognoses should be reevaluated as needed.⁴⁷

In all cases in which RRT is withheld or withdrawn, physician should provide adequate End-of-life comfort care through non-dialytic therapy even for critically ill patients in the ICU.⁶⁴ For patients with a death prognosis, different approaches other than integrating palliative care with intensive care treatment should be adopted. Indeed, in these conditions, palliative care may be replaced by hospice care.¹ In patients with terminal prognosis, the strategies to ensure a good death often involve more than effective analgesia and, ideally, should aim at optimizing comfort and dignity for the patient and at offering the opportunity of a close support from the family. Allowing patients to die in their own homes is a way of providing this.⁶⁵ Unfortunately, many patients suffer prolonged dying in hospitals, receiving unwanted, expensive and invasive treatments which may cause additional discomforts, such as pain, dyspnea, thirst and anxiety.⁶⁶

New developed technologies, such as wearable artificial kidney, should be taken into consideration for hospice care in nephropathic patients. Although this concept may be hardly applied in daily clinical practice, it may be potentially useful in home care management even for patients with AKI. This miniaturized, wearable technology may allow the maintenance of mechanical support, mainly through continuous ultra filtration. By improving fluid overload and reducing dyspnea, the wearable artificial kidney may provide human basic needs in end-of-life care⁶⁰ even, with adequate support, at patient home.

CONCLUSIONS

Palliative care is usually limited to seriously ill patients at the end-of-life phase and is often wrongly interchanged with hospice care. An earlier utilization of palliative care for all seriously ill patients may improve the quality of life of the patients and their families. Nephropathic patients usually present a decrease in life expectancy and may benefit from palliative care.

Although limited to end stages of the renal disease, the concept of palliative care is still better defined for CKD than AKI patients. Indeed, several therapeutic strategies may be attempted to improve Quality of life of chronic nephropathic patients, such as palliative dialysis, conservative management and PD. All these approaches require a tight collaboration between different healthcare professional figures, patients and their families. Prognosis, realistic treatment goals and therapeutic decisions should be shared among all subjects involved in the management of CKD. On the other hand, poor literature data are available on the effects of palliative and hospice care in patients with AKI. A methodological, ethical and clinical effort needs to be made to improve knowledge and awareness on palliative care in acute nephropathic patients.

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