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How to Manage Elderly Patients with Chronic Renal Failure: Conservative Management versus Dialysis

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Key Words
Chronic kidney disease · Elderly · Uremia · Low protein diet · Dialysis

Abstract
Over the past decade the number of elderly patients reaching end-stage renal disease has more than doubled. A fundamental medical decision that nephrologists commonly have to make is when to start dialytic treatment in elderly patients. Evidence is needed to inform about decision-making for or against dialysis, in particular in those patients frequently affected by multiple comorbidities for which dialysis may not increase survival. In fact, this decision affects quality of life, incurs significant financial costs, and finally mandates use of precious dialysis resources. The negative consequence of initiating dialysis in this group of patients can be deleterious as elderly people are sensitive to lifestyle changes. Furthermore, among dialysis patients, the elderly suffer the highest overall hospitalization and complication rates and most truncated life expectancy on dialysis of any age group. Studies of the factors that affect outcomes in elderly patients on dialysis, or the possibility in postponing in a safe way the start of a dialytic treatment, were lacking until recent years. Recently in the literature, papers have been published that address these questions: the effects of dialysis on morbidity and mortality in elderly patients and the use of a supplemented very low protein diet (sVLPD) in postponing the start of dialysis in elderly. The first study demonstrated that, although dialysis is generally associated with longer survival in patients aged >75 years, those with multiple comorbidities, ischemic heart disease in particular, do not survive longer than those treated conservatively. The second one is a randomized controlled study that compared a sVLPD with dialysis in 112 non-diabetic patients aged >70 years. Survival was not different between the two groups and the number of hospitalizations and days spent in hospital were significantly lower in those on a sVLPD. These studies add to the limited evidence that is currently available to inform elderly patients, their carers and their physicians about the risk and the benefit of dialysis. Copyright © 2008 S. Karger AG, Basel

The number of elderly patients with chronic kidney disease (CKD) stage 5 is steadily increasing [1]. In fact, more elderly patients are reaching end-stage renal disease due to both the increasing longevity of the general population and the important improvements in the treatment of cardiovascular disease and cancer.

In many cases, the nephrologists and patients themselves find it difficult to decide whether long-term dialysis is the best choice, especially when patients have multiple comorbidities, particularly heart failure, diabetes, and vascular diseases. As old age and comorbidities are predictors of mortality in elderly patients on dialysis, will dialysis prolong life? If so, will it be at the expense of quality of life? Evidence is needed to inform about decision-

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making for or against dialysis, especially in those patients with many risk factors for whom dialysis will not increase survival, and in elderly persons [2, 3].

About 50% of new dialysis patients are >65 years of age [4] and often suffer from comorbidities that may impair intradialytic cardiovascular stability and reduce the likelihood of maintaining a well-functioning dialysis vascular access; both of these factors increase morbidity in dialyzed patients. Functional dependence, impaired intellectual status, diabetes, low serum albumin, and late referral for end-stage renal disease treatment are also poor prognostic factors in this setting [5–8].

For each patient, the decision to commence dialysis or to have conservative management (prolonged low protein diet or palliative therapy) is complex. It is important to recognize that conservative management, without dialysis, is not simply defined by the absence of dialysis provision: it entails active disease management, for example active treatment of anemia, acidosis, or fluid balance, and detailed supportive care, which often becomes increasingly complex towards the end of life. Prognosis, anticipated quality of life, treatment burden if dialysis is undertaken, and a patient's preference play a part in the decision for or against dialysis.

For nephrologists or families the decision becomes increasingly challenging in older patients, not because age per se precludes dialysis, but because considerations of comorbidities, reduced overall lifespan and the impact of dialysis itself on quality of life become more complex with increasing age. Factors influencing the decision for starting dialysis, such as length of survival, determinants of survival, quality of life and disease burden have all been studied in elderly patients, and there are sufficient data on survival [9–16]. On the contrary, there is little comparative data on morbidity and mortality once the decision has been made. Two recently published studies have addressed this question [17, 18]. The aim of these studies is not to elucidate the factors influencing the dialysis decision-making, but, instead, to evaluate survival once the decision for or against dialysis has been made, and how to treat patients in a conservative management.

The study by Murtagh et al. [17] describes and compares survival in CKD5 patients >75 years managed with dialysis or conservatively, and tried to identify which of several key variables could be independently associated with survival. Patients were identified by using the clinical data base at four major renal units in the South Thames Region. All patients >75 years of age receiving dedicated multidisciplinary predialysis care, during a 12-month period, and who had chosen dialysis or conservative management were enrolled in the analysis. Dedicated multidisciplinary predialysis care was provided by a team of physicians, specialist nurses, counselors and dieticians providing additional educational, dietary, social and psychological support. Late referral patients were excluded from the analysis. In comparison with general nephrology care, the dedicated multidisciplinary care requires more time and more resources for education and psychosocial support. The final decision about dialysis was made jointly between each patient and nephrologists, based on the patient's wishes and suitability for dialysis. In any case, even in patients with a limited prognosis (such as in advanced metastatic cancer) who wished to have dialysis, the treatment was initiated. Patients were enrolled in the study when estimated GFR (eGFR) reached 15 ml/min. The primary outcome measure was survival from the time at which an eGFR of <15 ml/min was reached. In the study, 129 patients fulfilled the inclusion criteria: 52 elected to undergo dialysis, and 77 chose conservative management. Gender, ethnicity, cause of CKD and comorbidity score were not significantly different between the two groups, but the latter was older (median age 83.0 vs. 79.6 years, $p < 0.001$). Kaplan-Meier analysis confirmed that survival was better in patients who opted for dialysis than in those who chose conservative management ($p < 0.001$), but this was not the case when analysis was performed only in patients who had a high Davies comorbidity score, i.e. 2 or more risk factors [21]. In this case the difference was almost zero ($p = 0.98$). In particular, the analysis revealed that choosing dialysis over conservative treatment offered a significant survival advantage in patients with ischemic heart disease ($p = 0.27$). This study showed that survival was better in patients aged >75 years treated by dialysis versus patients treated conservatively, but not in those with a high comorbidity score, in particular when they suffered from ischemic heart disease.

Based on these data, in elderly patients, comorbidity, and especially ischemic heart disease, should be a key consideration in dialysis decision-making. In other words, in patients affected by several comorbidities, nephrologists or clinicians need to consider whether dialysis offers sufficient survival benefit and consider it a standard treatment or whether non-dialytic management may offer comparable survival without the treatment burden of dialysis.

Further support for a conservative management to starting dialysis in the elderly comes from a randomized controlled study performed in Italy [18]. In this study, the

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authors compared the morbidity and mortality in elderly patients (>70 years) randomized to a supplemented very low protein diet (sVLPD) or dialysis when their GFR reached the level of 5–7 ml/min, a value far below that suggested for starting dialysis by current guidelines [19, 20]. Patients with diabetes, acute life-threatening diseases, HIV infection or liver failure were excluded from randomization. 122 patients fulfilled the criteria for randomization, 56 were randomly assigned to sVLPD and 56 to dialysis. The sVLPD is a vegan diet, calorie intake is 35 kcal/kg b.w./day and protein intake is 0.3 g/kg b.w./day, supplemented with a mixture of keto-analogues and amino acids (100 mg/kg b.w./day) and group B vitamins. Patients on a diet started dialysis in the case of malnutrition, hyperkalemia, intractable fluid overload, or appearance of uremic symptoms. Median time following a sVLPD was 10.7 months (range 1.0–58.1); at the end of the study, 50% of diet patients and 55% of dialysis patients were dead. 10 very old patients (mean age 87.6 years, range 82–96) died while on the diet. 40 patients (71%) in the diet group started dialysis after a median of 9.8 months following a sVLPD (range 6.0–20 months). Survival was tested using intention-to-treat analysis (patients were considered part of the diet group even after the switch to dialysis) and per-protocol analysis (diet group patients were censored when switched to dialysis). At 1 year, survival rates were 83.7 and 83.9% in the dialysis and diet group, respectively. The analysis showed that survival in the diet group was not inferior to that in dialysis patients over the first 12 months of treatment, even without taking into account baseline differences (age and cerebral vasculopathy) that were disadvantageous for diet patients. The number of hospitalizations and days of hospitalization per patient-year were significantly lower in the diet group: 57 and 66% of those of the dialysis group, respectively. This difference was caused mainly by dialysis access-related complications. The diet enabled delaying placement of vascular access; in this way the related complications were reduced. The number of hospitalizations was 1.1 in the dialysis group versus 0.6 in the diet group ($p < 0.001$), whereas days of admission/patient per year were 11.0 versus 5.2 ($p < 0.02$). The hazard risk for hospitalization was significantly greater in the dialysis group (HR, 1.50; $p < 0.01$). No important difference was seen in causes of hospitalization except for dialysis access complications (0.31 admission/patient-year in the dialysis group versus 0.15 for the diet group) and fluid overload (0.13 vs. 0.05). Moreover, the authors remark that all the admissions caused by fluid overload in the diet group occurred only when following a sVLPD. It seems that patients following a sVLPD may learn over time to limit salt and fluid intake and self-check for signs of overhydration. The lower hospitalization rate in the diet group was not caused by more frequent clinic visits. Conversely, clinic visits were scheduled every 4–5 weeks for the diet group, whereas patients on hemodialysis were visited by a physician at every dialysis treatment, in other words 13–15 times in the 4- to 5-week period. Fewer accesses to the hospital was one more point in favor of diet in managing elderly uremic patients because it decreased both family and psychosocial burdens and had a less detrimental effect on quality of life. This result needs to be highlighted because patients were very old and with very advanced CKD, but it was possible to manage them in an outpatient clinic.

Baseline GFR in the patients randomized in the study was 32% of that of patients in the Modification of Diet in Renal Disease Study 2 (GFR in MDRD: 18.5 ml/min) [22]. The latest GFR level in the 40 patients switched from diet to dialysis was 4.3 ± 1.1 ml/min (range 2–7). In this selected population, not including patients with diabetes or nephrotic syndrome, the start of dialysis was done when the value was far below the suggested value by current guidelines. Furthermore, no patient showed signs of malnutrition, confirming previous findings and allying fears about protein-energy malnutrition [23]. These results indicate that a sVLPD compared with maintenance dialysis treatment in not less effective for preserving life for some time in older patients who are willing to accept a sVLPD.

This study does not suggest that start of maintenance dialysis treatment can or should be postponed by diet in all elderly uremic patients. Rather, for patients satisfying the selection criteria of the protocol and willing to follow a sVLPD, the start of dialysis can be delayed for at least 1 year without increasing the risk of either mortality or morbidity. Furthermore, in late referral patients who do not need urgent dialysis, the diet could allow time to plan the creation of a vascular access, or the position of a catheter for peritoneal dialysis, and wait until the start of the treatment can be done in a safe way. Postponing dialysis treatment should be cost-saving in countries where the number of elderly and very compromised patients with CKD5 is continuously growing. The dialysis treatment in this population is causing enormous costs. A conservative management or a sVLPD therapy could offer a temporary but valuable alternative to renal replacement therapy that could benefit both patients and our overburdened healthcare systems.

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Similar considerations can be applied to developing countries where dialysis treatment is not widely available and many patients are not treated. In this area, diet is largely based on rice and vegetables, two main components of the sVLPD. The cost of the keto-analogues and amino acid supplements is low compared to dialysis; in this way we can offer an opportunity of treatment for many patients.

In a small study (follow-up was 2 years) including 10 patients randomized to a sVLPD (0.3 g of vegetarian protein/kg b.w./day) and 10 to a diet containing 0.6 g of protein/kg b.w./day, the effect of these two regimens on erythropoietin responsiveness was addressed. The responsiveness improved in the sVLPD and was found to be inversely related to the level of parathyroid hormone. The levels of the hormone probably decreased in response to the drop in phosphate intake, potential phosphate binding by the keto-analogue's calcium salt, and the subsequent reduction in serum phosphate concentrations [24]. Furthermore, only 2 patients in the sVLPD reached the endpoint (start of dialysis treatment), whereas it was reached by 7 patients in the group on 0.6 g of protein/kg b.w./day, with a statistically significant difference ($p = 0.03$).

A preliminary analysis based on the Italian standard cost of dialysis, excluding the costs for hospitalization, showed that 1 patient per year on dialysis costs at least EUR 25,000 (bicarbonate dialysis), whereas 1 patient per year on a sVLPD costs EUR 5,000 [pers. unpubl. data]. If we consider that the hospitalization rate was lower in the group of diet patients, it is possible to calculate the cost saving even if only one fourth of our elderly patients reaching the end stage of renal function are treated in this way.

Patients with CKD should adhere to a detailed dietary care plan during their lifetime. A nutritional survey is highly recommended to verify that sufficient energy is provided in order to prevent the appearance of energy-protein malnutrition. Recent published data seem to suggest that, at least in selected elderly patients affected by CKD5, it is possible to postpone the start of dialysis reducing the burden of this therapy in patients themselves and families. Furthermore, this way of managing patients can reduce the high social and medical costs of this therapy, and, in very sick patients, there are data suggesting that a conservative management could be considered. A conservative management does not imply 'not for care', but rather active disease management and detailed supportive care right up to the very end of life.

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