# In Good Conscience—Safely Withholding Dialysis in the Elderly

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**ABSTRACT**

Across the world, the incidence of end-stage kidney disease is increasing in the elderly. However, they do not always fare very well on renal replacement therapy. Age at the start of dialysis, multiple comorbidities (especially if ischemic heart disease is one of them), diabetes, functional dependence, poor intellectual capacity, low serum albumin, peripheral vascular disease, and late referral have been associated with increased mortality on dialysis in various studies. Moreover, renal failure is only one of the many problems affecting the elderly and dialysis can potentially impair their quality of life tremendously. Therefore, it is often a challenge for the nephrologist to decide whether starting dialysis is in the best interest of the elderly patient. Is it sometimes nobler to provide supportive care without dialysis to an elderly patient with renal failure? Can dialysis be safely delayed where the nephrologist is uncertain of the prognosis or the patient is unsure whether or not to have dialysis? How robust is the evidence base to help inform discussion between the nephrologist and the patient/carer? What are the limitations in carrying out further research in this area? What does conservative management, which is better termed nondialytic supportive care, entail and how should it be delivered? This article aims to answer these fundamental questions confronting the nephrologist in day to day clinical practice.

To dialyse or not to dialyse, that is the question. When is it nobler to provide supportive care without dialysis for elderly patients with end-stage renal disease? What evidence can be called upon to justify these decisions? And indeed, whose decision is it anyway? This article attempts to provide some answers to these fundamental questions which confront nephrologists in everyday clinical practice.

## The Context

The incidence of end-stage renal disease (ESRD) in the elderly continues to increase because of the increasing longevity of the general population and improvements, over the last few decades, in the management of cardiovascular diseases, cancer and other diseases. In the United States, there has been a 67% increase in the incidence of ESRD in the over 75 years age group between 1994 and 2004 (1), the highest acceptance rate on to dialysis being in people between 75 and 84 years (2). In the UK, as in most European countries, 50% of patients starting dialysis are over the age of 65 years. In England and Scotland the incidence rate is highest in the 75–79 years age group, while in Wales and Northern Ireland the peak is between 80 and 84 years (3,4).

This enlarging body of "geriatric" ESRD patients has unique sets of problems that require specialized knowledge. Renal failure is only one of the many conditions affecting them and one also needs to be aware of their social problems (5). Moreover, they do not always fare well on renal replacement therapy. It is often a challenge for the nephrologist to decide whether starting dialysis is indeed in the patient's best interests, especially when there are multiple comorbidities. Will dialysis prolong life? If it does, will it be at the expense of quality of life?

## The Evidence

In studies examining factors affecting survival of elderly patients on dialysis, age at start of dialysis and multiple comorbidities have been implicated most often (6,7). The most notable of these is a recent study showing dialysis might not offer a survival benefit in patients over 75 years of age with multiple comorbidities, especially if they have ischemic heart disease (8). Functional dependence, impaired intellectual status, diabetes, low serum albumin, peripheral vascular disease, and late referral for ESRD treatment are also poor prognostic factors in this population (9,10).

People have attempted to stratify the risk of early death in elderly patients on dialysis on the basis of

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various risk factors. Stratification to low, medium, and high risk of death have been proposed on the basis of comorbidity scores (11,12). Recently, a French group has developed a clinical scoring system to predict early death on dialysis in the over 75 years age group using data from the French Rein registry. Their system takes into account all the risk factors independently associated with increased risk of death at 6 months in their cohort–diabetes, low body mass, congestive cardiac failure, peripheral vascular disease, dysrhythmia, active malignancy, behavioral disorder, dependency for transfers, and unplanned dialysis. Interestingly, unlike other studies, there was no correlation between age and early mortality (<6 months) on dialysis. The mortality varied from 8% in the lowest risk group (0 point) to 70% in the highest risk group (≥9 points) (13). These studies help inform any discussion between nephrologists, patients, and their carers about risks and benefits of dialysis in the elderly population.

While outcomes may (or may not) be poor for the elderly on dialysis, the relevant question for our purposes is the relative outcomes for these patients with and without dialysis. No large study has compared outcomes of conservative management with dialysis treatment in a matched control group. Joly et al. compared 43 octogenerians who were conservatively managed at the Necker renal unit in Paris with 107 patients of the same age group who were treated with dialysis over the same period of time. The median survival was 28.9 months in the dialysis group compared with 8.9 months in the conservative management group ($p < 0.0001$). However, the conservatively managed patients were far more likely to be socially isolated, diabetic, have low Karnofsky performance scores, and have a late referral rate (9). Of note, in this study, 37 of the conservatively treated patients were deemed unfit or unsuitable for dialysis by the nephrologist and only seven chose not to have dialysis.

Our own experience, albeit in a much smaller study, was different. We analyzed the outcomes of 38 consecutive patients from our multidisciplinary predialysis clinic who were aged over 75 years and had multiple comorbidities. The 19 patients who chose conservative treatment did not differ from the 19 who started dialysis in terms of age, gender, diabetes status, or level of comorbidity. Thus, our patient groups were much more comparable than those of the Necker groups. The dialysis group had more hospital admissions (14 vs. 5; $p = 0.008$), episodes of infection (8 vs. 0; $p = 0.003$), and deaths (7 vs. 2; $p = 0.12$) than did the conservative treatment group during 1 year of follow-up, although the last difference was not significant (14).

## The Limitations to the Evidence and Available Research Strategies

There are significant practical and ethical limitations on conducting research in this area of clinical practice. A randomized controlled trial of dialysis vs. conservative therapy, in which patients who are able and willing to give consent to receive either real or sham dialysis for a prolonged length of time, is not likely to survive ethics committee scrutiny. Even if it did, it would likely exclude those most elderly and vulnerable patients who have multiple comorbidities–just the group of patients in whom difficult decisions about whether or not to start dialysis have to be made in everyday practice.

Observational studies are based in everyday clinical practice potentially making their results more applicable to the wider population. However, the associations between patient characteristics, treatment interventions, and outcomes revealed by these studies do not necessarily imply a causative link between the treatment and the effect. As explained in detail in a recent review by Greene, observational studies are very prone to bias (15). The most important bias in studies comparing dialysis against conservative therapy is treatment-by-indication bias. Patients who receive supportive therapy but do not start dialysis are more likely to have greater comorbidity and psychosocial burden and so be biased towards having a worse outcome compared with those who receive dialysis. Statistical methods can be employed to adjust for differences in patient-related confounding variables between the two groups. However, it cannot be known for certain whether all the confounding factors have been identified, measured, and adjusted for adequately.

Observational studies employing more reliable statistical methods are urgently needed. Two methods being increasingly used are propensity scoring and instrumental variable analysis. In the former, the probability of an individual being offered a particular treatment is calculated based upon measurable demographic and comorbidity covariates. This propensity score is then used to adjust comparisons between the two study groups. However, this adjustment is only valid when the decision to assign an individual to a particular treatment is independent of the treatment outcome and so does not overcome the problem of treatment by indication bias in the use of dialysis.

Across the world, physicians in nephrology clinics differ greatly in their use of dialysis in certain groups of patients, such as the very elderly (16). This wide variation in clinical practice can be exploited as a kind of natural experiment using the "instrumental variable" study design.

If dialysis is delivered in a broadly similar way, the particular clinic in which patients receive treatment is unlikely to significantly affect their outcome. If a theoretical cohort of similar elderly patients with ESRD were randomly allocated to a number of different physicians or clinics, their outcomes would then be dependent upon whether or not the clinic in which they are treated starts them on dialysis. The clinic can thus be used as an instrumental variable, independent of the effect of the dialysis treatment itself on the patient's outcome.

In the real study, patients would be selected at random from a randomly selected number of representative clinics across the world. Associations could then be identified between the instrumental variable, i.e., the clinic's practice of starting dialysis, and mortality and quality of life outcomes of patients treated in that clinic. If sufficiently powered, the study would be able to reveal asso-

ciations between the practice of starting dialysis at different levels of eGFR within subgroups of patients, so providing clinicians and patients with evidence to support their decisions about treatment of individuals. A worked example of the instrumental variable approach has been published from the Dialysis Outcomes and Practice Patterns Study (17).

In actuality, the question of whether dialysis will benefit the patient is really not an absolute one. Rather, it is determining the level of remaining GFR at which such benefits exceed the problems associated with implementing and maintaining the treatment. Clearly, the risk:benefit ratio becomes quite low as anuria approaches. However, in patients with GFRs in the 5–15 ml/minute range, avoiding dialysis in those destined to die regardless of dialysis therapy would likely be beneficial. The crux of the problem is selecting those patients whom the finger of fate has selected for a nonrenal demise during the terminal decline in renal function.

## The Practical Implications–What Is Best Practice in Conservative Care?

How does dialysis affect quality of life in the elderly? In the very elderly ( > 75 years) quality of life perhaps is more important than the quantity. "Dialysis should add life to years rather than years to life" (18). The few studies that have looked at quality of life showed that health related quality of life in the elderly dialysis patients is as good, if not better, as in the younger dialysis patients (6,19,20); modality of dialysis does not matter (21). However, there is not a single study that has compared quality of life between a cohort of conservatively managed patients and a matched control group on dialysis. Since for most elderly patients peritoneal dialysis is not an option, hemodialysis becomes the modality of choice by default. The traveling time from dialysis centre, the long hours spent on the dialysis machine, the postdialysis "unwellness," the missed meals, access complications, and coming home to care for themselves can potentially affect their quality of life tremendously.

Therefore, an elderly patient who has significant functional impairment and mutiple comorbidities, especially ischemic heart disease, could have little to gain from dialysis. A conservative approach, with the informed consent of the patient and the carer, may be more appropriate in this setting. Conservative management does not simply mean nondialytic management of kidney failure; it entails active disease management–treatment of anemia, acidosis, fluid balance, and active end of life care. This requires a multidisciplinary approach to help elderly patients achieve the best possible quality of life. This also requires integration of services with primary care, community nurses, and the palliative care team so that the patients can be cared for at home until their death (if this is the patient's choice) or late initiation of dialysis. Such a late initiation of dialysis must not be considered a failure to plan properly or provide appropriate care if it is based on a thoughtful approach to an individual patient's situation.

A recently published prospective study from the UK of elderly patients with ESRF who were managed conservatively by a multidisciplinary team showed a median overall patient survival of 1.95 years with a 1-year survival rate of 65%. Stoke comorbidity grade (22) was an independent predictor of length of survival. More importantly, 60% of these patients did not have any hospital admissions over the observation period of 3 years and 71% of the patients who died, did so at home (23).

Further support for nondialytic management in the elderly comes from an Italian study, which looked at the effect of a very low protein diet supplemented with ketoanalogs, aminoacids, and B vitamins (sVLPD) on morbidity and mortality in nondiabetic elderly patients ( > 70 years) with ESRF. They randomized 122 patients with eGFR between 5 and 7 ml/minute to receive either sVLPD or dialysis. As per protocol, patients in the diet group started dialysis in case of severe hyperkalemia, intractable fluid overload, uremic symptoms or if they developed signs of malnutrition. One year observed survival rates were 83.7% in the dialysis group against 87.3% in the sVLPD group (log-rank test for noninferiority, $p < 0.001$ in an intention to treat analysis). The numbers of hospitalizations and days spent in hospital were significantly lower in the sVLPD group than in the dialysis group with a hazard ratio for hospitalization of 1.5 for the dialysis group (95% CI, 1.11–2.01; $p < 0.01$). In total, 71% of patients on the very-low protein diet started dialysis, after a median of 9.8 months (range 6–20 months) on sVLPD, and 18% died while still on the diet; 11% remained on the diet at 16.6 months (range 14.7–41.8 months). The authors concluded that sVLPD was effective and safe in postponing dialysis treatment in the elderly patients without diabetes (24). The safety and efficacy of very low protein diet in slowing progression of chronic kidney disease and delaying onset of renal failure were suggested by a meta-analysis done more than a decade ago and the secondary analysis of the Modification of Diet in Renal Disease (MDRD) study (25,26).

## The Practical Approach

Research evidence only gives general guidance, at best, about categories of patients, not about individuals. Decisions about starting dialysis need to be made in a partnership between the doctor (specialist and GP), the patient, and the family/carers. The nephrologist's role is to provide objective advice based upon the best available evidence and then to support the patient in their choice once it has been made.

Patients should be given an estimate of his or her likely future on dialysis. We now have a good body of evidence to suggest that advanced age, male gender, decreased serum albumin, malnutrition, impaired functional status, diabetes mellitus, and coronary heart disease are poor prognostic factors. In patients with stage five CKD who have multiple poor prognostic factors, especially if one of those is coronary artery disease, dialysis might not offer a survival advantage (27). Moreover, quality of life is a strong predictor of mortality, even

after statistical correction for these comorbid factors (28).

In an individual patient whose prognosis is particularly uncertain, or in the case of a disagreement between the views of the nephrologist and the patient and/or the carer, a time-limited trial of dialysis may be offered (29). This will enable the patients and his or her family an insight into what life on dialysis entails. This will also give sufficient time for further discussion between the nephrology team, and the patient and their carer.

Most nephrologists would agree that patients who are likely to have an unacceptable quality of life should not be subjected to the discomfort of dialysis. Sparing such patients the inconvenience and discomfort of hospital attendances, surgical access procedures, and dialysis treatments is a major benefit.

Many of the symptoms and complications of kidney failure, e.g., anemia, acidosis, pruritus, insomnia, depression, fluid overload, and hypertension, can be treated with medication. Moreover, we now have evidence that very low protein diet allows safely delaying start of dialysis until eGFR drops to 5 ml/minute or lower. These measures allow time for decision making where either the patient is unsure about having dialysis or the nephrologist is uncertain about the prognosis. However, if severe hyperkalemia, intractable fluid overload, uremic symptoms, or signs of malnutrition supervene, the nephrologist and patient may decide to start dialysis sooner.

Should the patient chose not to have dialysis or the nephrologist decides, in conjunction with the patient and his or her carer, that dialysis treatment will not be of benefit, they should be offered maximum supportive care. The option of not having dialysis should not deny the patient any other supportive care–epoetin, pain control, dietetic, psychological, and social care support. It is best delivered as part of a holistic service provided by an integrated kidney failure specialist team. The multidisciplinary team should have active links with the palliative care specialists so that there is a smooth transition from active medical management to terminal care.

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