

Renal Failure >

Volume 29, 2007 - [Issue 6](#)

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Factors Affecting Survival in Advanced Chronic Kidney Disease Patients Who Choose Not to Receive Dialysis

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Pages 653-659 | Published online: 07 Jul 2009

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Abstract

Introduction. Non-dialytic treatment (NDT) has become a recognized and important modality of treatment in end stage renal disease (ESRD) in certain groups of chronic kidney disease (CKD) patients. However, little is known about the prognosis of these NDT patients in terms of hospitalization rates and survival. We analyzed our experience in managing these NDT with a multidisciplinary team (MDT) approach over a three-year period. **Patients and Methods.** The Renal Unit at the Royal Liverpool University Hospital set up a dedicated MDT clinic to manage NDT patients in January 2003. Patients approaching end stage chronic kidney disease who chose not to dialyse were recruited from other nephrologists. The study group was classified according to age band (<70 years, 71-80 years, and >80 years), estimated glomerular filtration rate (eGFR) (<10

formula and Stoke comorbidity grade (SCG). The SCG is a validated scoring system for the survival of patients on renal replacement therapy. We also used the ERA-EDTA primary renal diagnosis codes. As there are no existing standards for NDT patients, we used the U.K. national set for haemodialysis patients as a reference and target for our NDT patients. Data was collected prospectively. Results. The median age was 79 years and the male: female ratio was approximately 1. The most common primary cause of kidney disease in the NDT study population was chronic renal failure of unknown cause $n = 22$ (31%), but the most common identifiable cause was diabetic nephropathy, $n = 20$ (28%). The most common comorbidity was ischaemic heart disease $n = 25$ (34%). Those achieving the standards for anaemia were 78% at referral. Only 30% of the NDT patients achieved the standard for blood pressure ($<130/80$ mmHg) at referral. Forty-three patients (60%) had no admissions at all. There were a total of 30 patients admitted on 58 occasions. Thirty-one (53%) of these were due to a non-renal cause. The median length of stay for the other NDT patients was 10 days. The median overall survival (life expectancy) was 1.95 years. The one-year overall survival was 65%. SCG was an independent prognostic factor in predicting survival in NDT patients studied ($p = 0.005$), the hazard ratio being 2.53, for each incremental increase in the SCG. At one year, the survival for comorbidity grade 0, 1 and 2 were 83%, 70% and 56% respectively. Of the 28 patients who died, 20 did so at home (71%). Discussion. The NDT of ESRD has become an important alternative modality in renal replacement therapy. With the emergence of epidemic proportions of CKD, more elderly patients with progressive renal disease will need to make informed decisions regarding renal replacement therapy. There is likely to be increasing number of elderly patients that will tolerate dialysis badly and who will be very dependent on others. We believe that there should be a multidisciplinary approach to assist the ESRD patients in choosing their modality of renal replacement therapy, and with an agreed care plan to support these patients in managing their chosen modality to achieve the best possible quality of life. There should be integrated services with primary care, community nurses, and palliative care teams to enable the majority of the patient's treatment to be carried out at home and to allow a dignified death. However, there was a statistically significant trend for shorter survival among those with greater comorbidities, as determined by the SCG. This is the first report of the potential importance of SCG as an independent prognostic factor in NDT patients. This will help us to counsel our patients in the future about their prognosis if they choose NDT as their modality of renal replacement therapy. Conclusion. Our prospective study is the first and currently the largest

patients. SCG was an independent prognostic factor in predicting survival. In those patients who chose not to dialyse, SCG provides a potentially useful indication of expected prognosis.

Keywords:

non-dialytic treatment

Stoke comorbidity grade

chronic kidney disease

multidisciplinary team

INTRODUCTION

Non-dialytic treatment (NDT) has become a recognized and important modality of treatment in end stage renal disease (ESRD) in certain groups of chronic kidney disease (CKD) patients. The UK Renal Association recommends that an informed and joint decision should be made between patient, family, and physician when determining the best modality of renal replacement therapy (RRT). A multidisciplinary team (MDT) approach is recommended to manage these NDT patients.[\[1\]](#) However, little is known about the prognosis of these NDT patients in terms of hospitalization rates and survival. We analyzed our experience in managing these NDT with a MDT approach over a three-year period.

AIMS OF STUDY

The aims of the study are as follows:

1. To evaluate the prognostic factors influencing the survival of NDT patients.
2. To evaluate the hospitalization rates and the survival rates in NDT patients and the clinical risk factors for these.
3. To evaluate if the Renal Association Standards (RAS) for renal anemia, renal biochemical parameters, and blood pressure are reached in practice in this population.

The Renal Unit at the Royal Liverpool University Hospital set up a dedicated MDT clinic to manage NDT patients in January 2003. The MDT comprised of a consultant nephrologist, renal dietician, anaemia specialist nurse, a ward link nurse, social worker, community nephrology nurse, and a complementary therapy practitioner. At clinic attendance, all members of the multidisciplinary team reviewed patients. The interval between clinic visits ranged from one week to three months, depending on clinical need. Every effort was made to reduce the frequency of attendance, and whenever possible the patients were reviewed in their own homes by the community nephrology nurse. The clinic has strong links with primary care and the palliative care team.

Patients approaching end stage chronic kidney disease who chose not to dialyze were recruited from other nephrologists. In some cases, the patients had been advised that dialysis was unlikely to result in a significant increase in length of life, due to associated comorbidity and dependency. In other cases, dialysis treatment had been recommended but declined. The study group was classified according to age band (<70 years, 71–80 years, and >80 years), estimated glomerular filtration rate (eGFR) (<10 mL/min, 11–20 mL/min, and >20 mL/min) according to the Modified Diet in Renal Disease (MDRD) formula and Stoke comorbidity grade[2],[3] (SCG). The SCG is a validated scoring system for the survival of patients on renal replacement therapy.[3] It is based on the presence of malignancy, ischemic heart disease, peripheral vascular disease, left ventricular dysfunction, diabetes mellitus, systemic collagen vascular disease or other significant pathology (e.g., COPD, cirrhosis, or psychotic illness). The grade, which ranges from 0 to 2, is determined by the number of comorbidities present.[3] Grade 0 equivalent to no recorded comorbidities; Grade 1, one to two comorbidities; and Grade 2, three or more comorbidities.

We also used the ERA-EDTA primary renal diagnosis codes. As there are no existing standards for NDT patients, we used the U.K. national set for hemodialysis patients as a reference and target for our NDT patients. Data was collected prospectively.

STATISTICAL METHODS

Cox regression multivariate analysis was used to study prognostic factors that may influence survival. Kaplan Meier method was used to compare survival between the groups according to age bands, eGFR, and SCG. STATA version 9 (College Station,

RESULTS

The demographics of the patients referred to the clinic between January 2003 and January 2006, and the hematological, biochemical, and clinical data at referral are shown in [Table 1](#). The median age was 79 years and the male: female ratio was approximately 1.

Table 1 Demographics and baseline parameters of non-dialytic treatment patients at referral

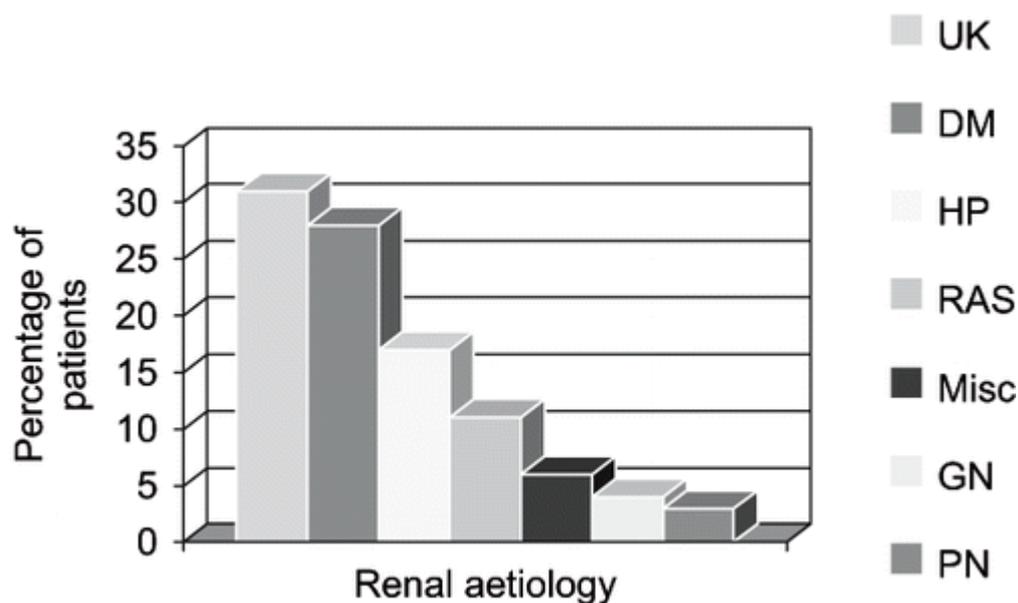
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The most common primary cause of kidney disease in the NDT study population was chronic renal failure of unknown cause, $n = 22$ (31%), but the most common identifiable cause was diabetic nephropathy, $n = 20$ (28%, see [Figure 1](#)). The most common comorbidity was ischemic heart disease, $n = 25$ (34%).

Figure 1. Primary causes of renal disease. Abbreviations: UK = Unknown, DM = Diabetes, HP = Hypertensive nephropathy, RAS = Renovascular, Misc = Miscellaneous, GN = Glomerulonephritis, PN = Pyelonephritis.



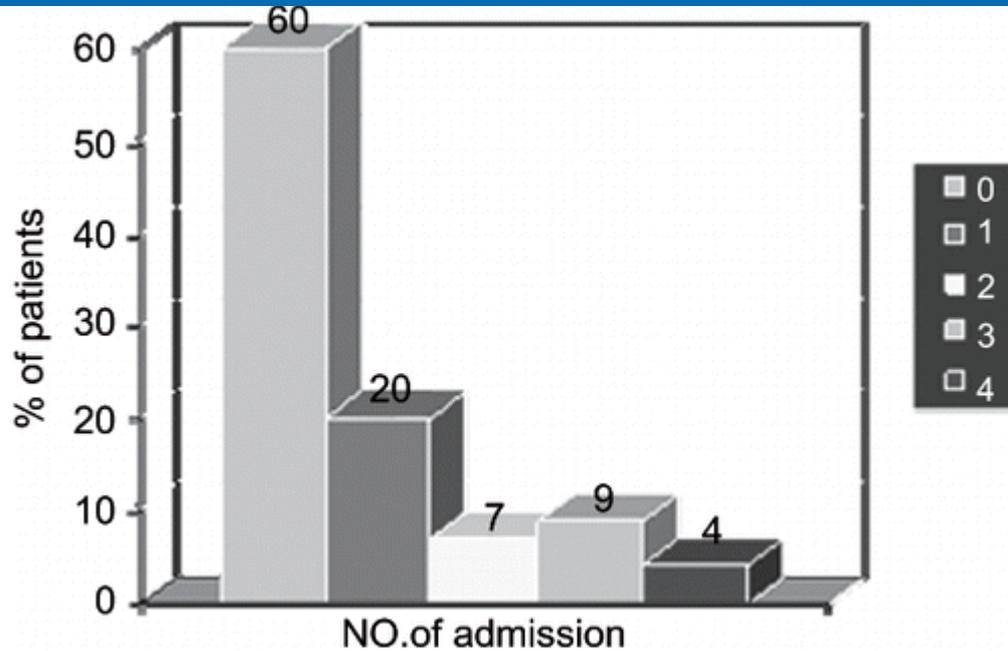
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Those achieving the standards for anemia (i.e., hemoglobin of above 10 g/dL within 6 months of seeing a nephrologist) were 78% at referral. Prior to being seen in the NDT clinic, only 59% of the patients had been seen by an anaemia nurse. As the anemia nurse saw more patients, the percentage use of intravenous iron sucrose and darbepoetin increased from 35% to 68% and 76%, respectively. This had a direct impact on hemoglobin, and the percentage of patients achieving standard reached 100% at 12 months in the NDT clinic.

Only 30% of the NDT patients achieved the standard for blood pressure (<130/80 mmHg) at referral, and this remained similar throughout, dropping to 25% at 3 months and back up to 29% at 12 months. We found that many of our patients could not tolerate the aggressive reduction in blood pressure, and a pragmatic approach was adapted to ensure a balance between the adverse effects of hypotension and achieving the target.

We used hospital admission rates as one of our quality standards for the effectiveness of the multidisciplinary team. Forty-three patients (60%) had no admissions at all (see [Figure 2](#)). There were a total of 30 patients admitted on 58 occasions. Thirty-one (53%) of these were due to a non-renal cause. Renal causes (defined as illness directly related to chronic kidney disease, such as uremic symptoms, hyperkalemia, or fluid overload) were responsible for the remaining 27 admissions. During the course of admission, three patients, two with severe uremic symptoms and one with pulmonary edema, elected to commence hemodialysis. These three patients all had prolonged, complex admissions with a median length of stay of 65 days. By contrast, the median length of stay for the other NDT patients was 10 days.

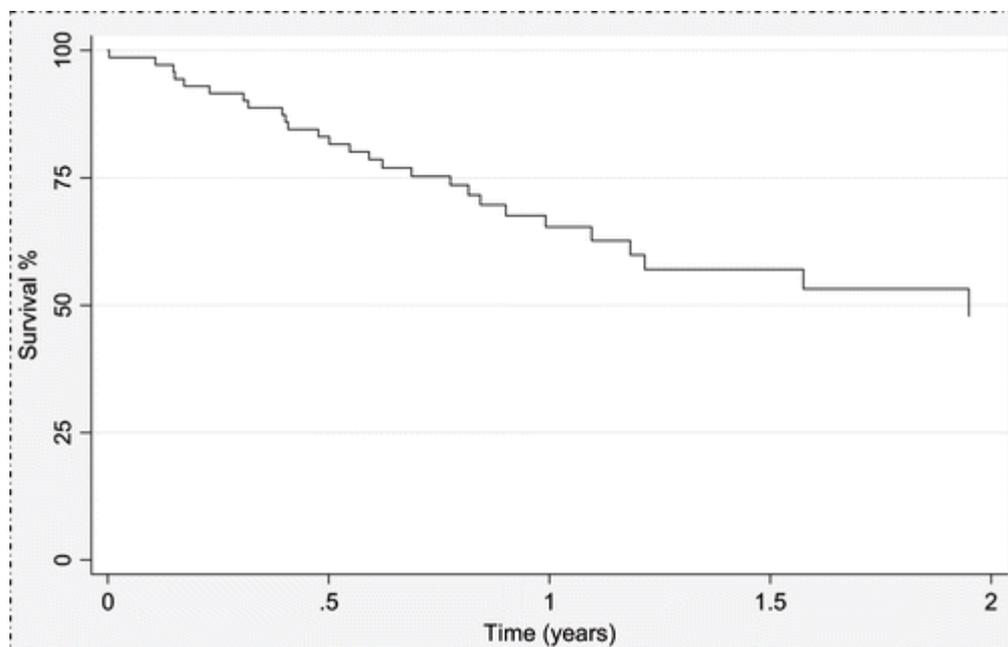
Figure 2. Number of hospital admissions.



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The median overall survival (life expectancy) was 1.95 years. The one-year overall survival was 65% (see [Figure 3](#)).

Figure 3. Kaplan-Meier curve showing overall survival of non-dialytic treatment patients.

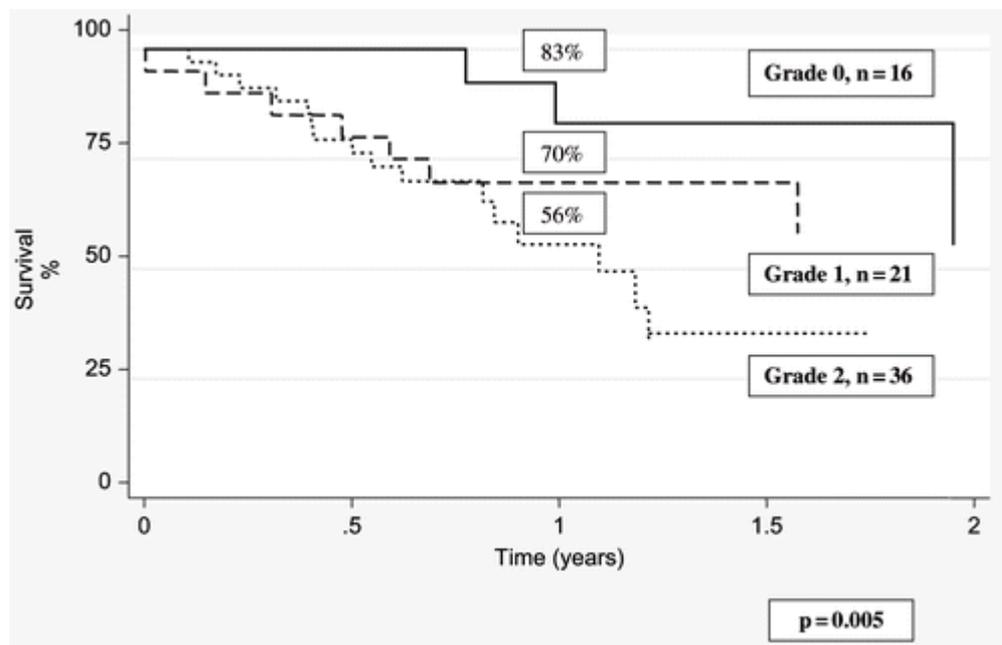


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The impact of a variety of clinic parameters on mortality was analyzed (see [Table 2](#)). SCG was an independent prognostic factor in predicting survival in NDT patients

incremental increase in the SCG. At one year, the survival for comorbidity grade 0, 1, and 2 were 83%, 70%, and 56%, respectively (see [Figure 4](#)).

Figure 4. Kaplan-Meier survival curve by Stoke's comorbidity grade.



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Table 2 Cox regression multivariate analysis: important prognostic factors for survival

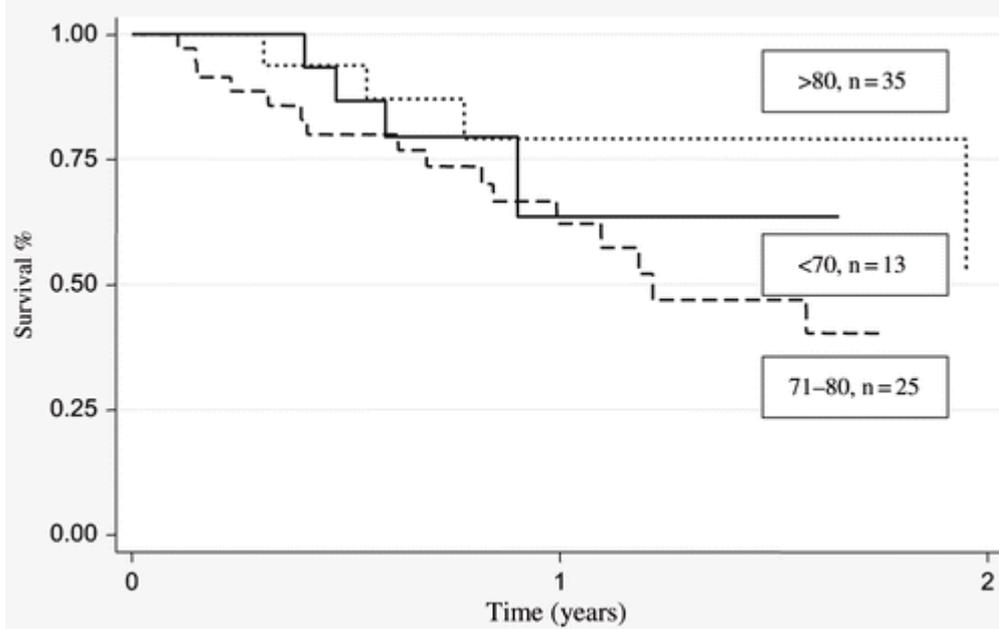


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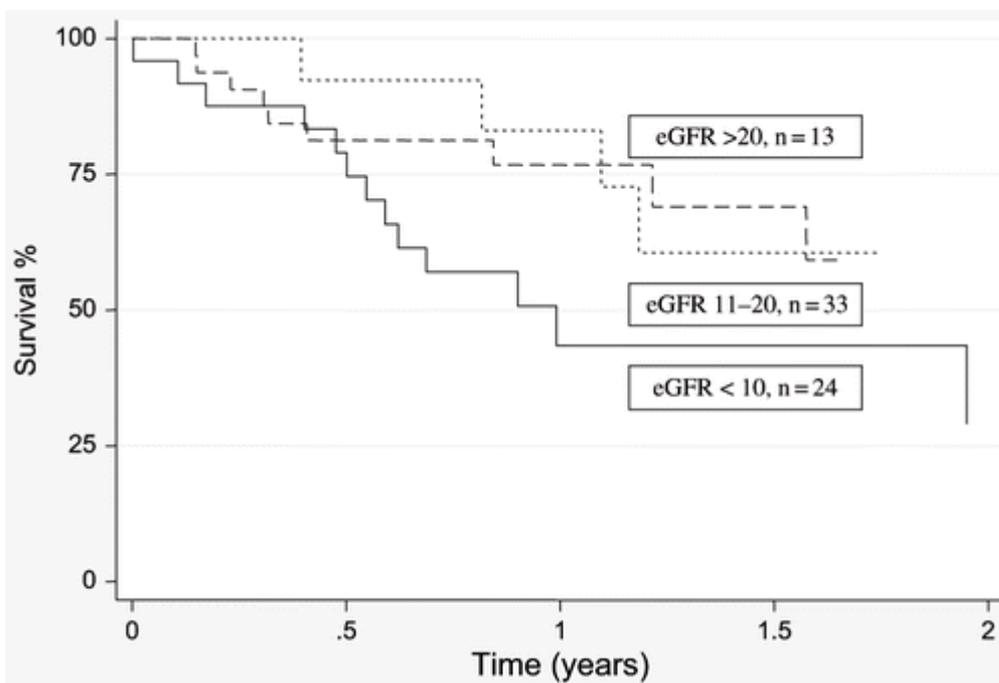
Age band (<70 years, 71–80 years, and >80 years) and eGFR (<10 ml/min, 11–20 ml/min, and >20 ml/min) were not independent prognostic factors, but there was a statistically non-significant trend for shorter survival with increasing age and lower eGFR at referral (see [Figures 5](#) and [6](#)). Similarly, hemoglobin (>10g/dL), calcium (2.2–2.6 mmol/L), and phosphate (<1.8mmol/L) were not independent prognostic factors. Patients with diabetes had decreased survival, but again this was not statistically significant.

Figure 5. Kaplan-Meier survival curve by age band.



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Figure 6. Kaplan-Meier survival curve by eGFR.



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Of the 28 patients who died, 20 did so at home (71%). All causes of death were confirmed by death certificates except for one patient, who died outside the UK of an unknown cause.

The NDT of ESRD has become an important alternative modality in renal replacement therapy. Between 1988–2004, the acceptance rate of ESRD treated by dialysis in the United Kingdom increased from 55 to 103 per million population.[\[4\]](#) With the emergence of epidemic proportions of CKD, more elderly patients with progressive renal disease will need to make informed decisions as regards renal replacement therapy. There is likely to be an increasing number of elderly patients that will tolerate dialysis badly and who will be very dependent on others.

Data from Chandna et al. found that highly dependent patients have very poor survival on dialysis.[\[5\]](#) Furthermore, the same authors reported that ESRD patients with poor functional status and extensive co-morbidities did not survive longer when dialyzed than when managed with NDT. Those that were dialyzed are more likely to be admitted and die in hospital.[\[6\]](#)

In the North Thames Dialysis Study of the elderly people on dialysis, approximately 50% of patients in the age band greater than 80 years old had died within the first year after commencing dialysis, compared to only 20% in the 70–74 years old age group.[\[7\]](#) In that study, age greater than 80 years old and peripheral vascular disease were significantly associated with increased mortality on dialysis. The observation that older dialysis patients do worse is not new and has been noted elsewhere.[\[8\]](#),[\[9\]](#)

In contrast, in a single center cohort in France with a 12-year observation period, octogenarians that underwent dialysis (n = 107) had a median survival of 28.9 months compared to 8.9 months in those with NDT (n = 37; p < 0.0001). The independent predictors of death within a year were poor nutritional status, late referral, and functional dependence.[\[10\]](#)

At present, there is no scoring system or clinical intuition that can accurately predict death soon after starting dialysis for ESRD. Therefore, limiting access to dialysis on the basis of likely short survival may be inappropriate.[\[11\]](#)

When discussing treatment options with patients approaching ESRD, we try to acknowledge the uncertainties outlined above. Despite these uncertainties, some patients will choose the NDT option. We believe that there should be a multidisciplinary approach to assist the ESRD patients in choosing their modality of renal replacement therapy, and with an agreed care plan to support these patients in managing their chosen modality to achieve the best possible quality of life. There should be integrated

majority of the patient's treatment to be carried out at home and to allow a dignified death.

There is a paucity of literature in the area of NDT of ESRD apart from studies described above.[\[6\]](#),[\[10\]](#) In this paper, we have shown that it is possible to achieve the standards used for dialysis patients for anemia and bone chemistry in the majority of NDT patients. This was done by treatment predominantly in the community with relatively infrequent visits to the hospital outpatient clinic. Patients managed this way have a median survival of nearly two years. Hospital admission rates were low, and many patients were able to die in the familiar surrounding of their own homes, rather than as hospital inpatients.

Age did not predict survival. There was a trend for those with a lower eGFR and with diabetes to have a shorter survival, although this was not statistically significant. However, there was a statistically significant trend for shorter survival among those with greater comorbidities, as determined by the SCG. This is the first report of the potential importance of SCG as an independent prognostic factor in NDT patients. This will help us to counsel our patients in the future about their prognosis if they choose NDT as their modality of renal replacement therapy.

Those patients who elected to commence dialysis did poorly with frequent early complications of dialysis and hospitalizations. These patients were effectively “late referrals” and had complications, particularly of dialysis line infections. Hence, while NDT patients retain autonomy and have the absolute right to change their minds and receive dialysis, it is important that when patients are accepted on an NDT program, they are aware that such a course may lead to a very difficult start on dialysis.

In conclusion, our prospective study is the first and currently the largest observational study of a multidisciplinary approach in the management of NDT patients. SCG was an independent prognostic factor in predicting survival. The overall median survival was 1.95 years; one year mortality was 35%. Over a three-year period, 60% of patients had no admissions at all, and more than 70% of the patients died at home. In those patients who chose not to dialyze, SCG provides a potentially useful indication of expected prognosis.

Statistical work was conducted by Patrick O'Kelly (MSc.), renal statistician, Beaumont Hospital, Dublin, Ireland. The authors would also like to thank Alexandra Mason, renal dietitian; Nancy Tanahill, specialist nurse for non-dialytic therapy; Andrea Anthoney, community sister and palliative care; Bernadette Rush, ward link nurse; and Debbie Shakespeare, social worker for their contribution in the multidisciplinary clinic.

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