Very Old Patients on Hemodialysis: How They Start and Can We Predict Survival?

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Key Words

Dialysis prescription · Elderly patients · Hemodialysis · Outcomes · Registry · Vascular access

Abstract

Background: We describe circumstances of dialysis initiation, dialysis prescription and factors affecting survival in elderly patients. **Methods:** We included all incident patients ≥ 80 years old from a National Registry for which clinical and laboratory data at dialysis initiation could retrospectively be obtained. **Results:** Of 170 patients included, 24% had diabetes, 30% ischemic heart disease, 13% peripheral arterial disease, 15% active malignancy and 60% prior nephrology care. Mean creatinine was $672 \pm 225 \mu\text{mol/l}$, eGFR $7.3 \pm 3.7 \text{ ml/min/1.73 m}^2$, 81% started dialysis in hospital and 78% with a catheter. 32% had <2 sessions/week and 29% had single-needle dialysis. One-year survival was 74% (median 26 months). In multivariate analysis only age (HR 1.10) and prior nephrology care (HR 0.48) were significant predictors of survival. **Conclusions:** The majority of elderly patients started dialysis with a catheter and in hospital setting. We estimate observed survival as good. Only age and prior nephrology care were independent predictors of survival.

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Introduction

The age of patients reaching end-stage kidney disease and requiring renal replacement therapy is increasing worldwide [1–4]. The proportion of elderly (age 65 and older) and very elderly (age 80 and older) patients in incident dialysis population is increasing as well and is likely to continue growing in the future, thus the term 'epidemic of aging' seems appropriate [1]. The expected survival of very elderly in the general population is considerable, but is significantly reduced by the presence of end-stage renal disease, significant comorbidities or frailty. Some patients at this advanced age might not benefit from initiation of dialysis and careful consideration is therefore justified [5]. A time-limited trial of dialysis or prolonged conservative management can be proposed [6] in agreement with the patient or the relatives [7]. As a result of these trends to more conservative treatment in the very elderly, an increase in withdrawal from dialysis in the elderly over the past years has been reported in some countries [8].

While there are many studies looking at the survival and prognostic factors in this very elderly population [9–11], little is known about the clinical circumstances in which these patients start dialysis and how they are being dialyzed, since this data is usually not registered in renal replacement therapy registries.

Table 1. Mean laboratory results and presence of comorbidities prior to first hemodialysis

Parameter	Value
Number of patients	170
Creatinine, $\mu\text{mol/l}$	672 ± 225
eGFR (MDRD), ml/min/1.73 m^2	7.3 ± 3.7
Urea, mmol/l	38 ± 10
Potassium, mmol/l	5.06 ± 1.01
Calcium, mmol/l	2.12 ± 0.29
Phosphate, mmol/l	1.94 ± 0.51
Hemoglobin, g/l	104 ± 15
Albumin, g/l^a	34 ± 7
Diabetes mellitus	24%
Ischemic heart disease	30%
Peripheral arterial disease	13%
Active malignancy	15%
History of malignancy	7%

Data is presented as mean $\pm$ SD or percentage. ^a $n = 93$.

The aim of our study was to describe the circumstances of initiating dialysis in very old patients and analyze factors influencing their survival based on data from a National Registry.

Subjects and Methods

We screened all incident (including day 1) patients ≥ 80 years of age from the Slovenian Renal Replacement Therapy Registry, who started hemodialysis between January 1, 2004 and December 31, 2010. We asked all dialysis centers to retrospectively obtain data from patients' charts regarding their clinical status and laboratory results prior to starting hemodialysis, either at the last outpatient visit or on the day of first hemodialysis in case of in-hospital start. We included in the final analysis all patients for which the majority of the requested data could be obtained.

The recorded comorbidities at dialysis initiation were: presence of diabetes mellitus, ischemic heart disease, peripheral arterial disease, active malignancy or history of malignancy (excluding skin cancers). The other parameters recorded were: whether the patient was seen by a nephrologist at least 3 months prior to dialysis initiation, vascular access at dialysis initiation, whether the patient was living at home or in a nursing home, and whether hemodialysis was started in an outpatient or in-hospital setting. Patients were followed until December 31, 2010, and the time and cause of death were obtained from the registry data.

Data regarding dialysis prescription was obtained from prospectively collected registry reports at the end of the calendar year in which the patient initiated dialysis; for the patients dying before the end of the first calendar year on dialysis, the data collected pertained to the week before death. The data collected included num-

Table 2. Other parameters at initiation of hemodialysis

Parameter	Value
Living at	
Home	80%
Nursing home	11%
No data	9%
Hemodialysis started	
In-hospital	81%
Outpatient	13%
No data	6%
Seen by nephrologist at least 3 months prior to starting dialysis	
Yes	60%
No	32%
No data	8%
Vascular access at first dialysis	
AV fistula	22%
Catheter	78%

ber of dialysis sessions per week, weekly duration of hemodialysis, single- or double-needle dialysis mode, whether the patient received epoetins and type of vascular access.

Data is presented as mean $\pm$ SD, median and interquartile range (IQR) or percentage, as appropriate. Survival rates were estimated with Kaplan-Meier survival analysis and survival was censored in case of recovery of renal function (4 cases); none of the patients were transplanted. Observed survival was compared to median life expectancy of the age- and sex-matched general population calculated from national statistics data. Uni- and multivariate Cox regression analysis was used to identify factors predicting survival. Statistical analyses were performed with SPSS version 10.0.5 (SPSS, Inc., USA). The study was approved by the National Medical Ethics Committee (Ref. No. 84/08/13).

Results

In the observed 7-year period, 1,713 patients (including day 1) started renal replacement therapy in Slovenia and out of them 214 (12.5%) patients were ≥ 80 years of age. Out of the 214 patients screened for inclusion, for 170 (71% response rate) additional clinical and laboratory data were obtained and were finally included in the study. Their median age was 83 (IQR 81–85) years and 49% were male. Most common primary renal diseases were: unknown (34%), nephrosclerosis (22%) and diabetic nephropathy (17%). Average laboratory results prior to starting dialysis and patients' comorbidities are shown in table 1, while other parameters at initiation of dialysis are

Table 3. Details of hemodialysis prescription at the end of first year on dialysis (or prior to death)

Dialysis mode	
Double-needle	64%
Single-needle	29%
No data	7%
Procedures per week, n	
3	62%
2	32%
1	0%
No data	6%
Weekly duration of dialysis, h	12 (8–12)

Data is presented as % or median and IQR.

shown in table 2. Out of the patients who were seen by a nephrologist at least 3 months prior to starting dialysis, 36% started with an AVF (vs. 2% of those not seen by a nephrologist, $p < 0.001$) and 71% started dialysis in hospital (vs. 95%, $p < 0.001$).

Dialysis Prescription

At the end of their first year on renal replacement therapy (or prior to death for patients not surviving by the end of the first year) all patients were treated with hemodialysis. Details of dialysis prescription are given in table 3. The majority of patients (88%) received epoetins. Vascular access at the end of the first year on renal replacement therapy (or prior to death) was AVF in 47%, catheter in 45% and data was missing in 8%. In comparison to the access at initiation of dialysis (table 2) this was a doubling of the prevalence of AVF by the end of the first year on hemodialysis.

Outcome and Predictors of Survival

In the observed period, 93 (55%) patients died and 4 patients recovered renal function. The cause of death was cardiovascular in 54%, unknown in 18%, infection in 16%, other in 7%, and malignancy in 5%. The Kaplan-Meier survival curve for the entire cohort is shown in figure 1. Median survival was 26 months, while 1-, 2- and 3-year survival rates were 74, 52 and 41%, respectively. Median life expectancy of the age- and sex-matched general population calculated from national statistics data would be 7.3 years. In univariate Cox regression analysis advanced age, higher phosphate levels and starting dialysis in hospital setting were all significant predictors of worse survival, while being seen by a nephrologist at least 3 months prior to dialysis initiation, starting dialysis with

Table 4. Results of univariate Cox regression analysis predicting patients' mortality

Parameter	Valid n ^a	Hazard ratio (95% CI)	p value
Age, years	169	1.13 (1.05–1.21)	0.001
Phosphate, mmol/l	141	1.66 (1.10–2.51)	0.02
Creatinine, $\mu\text{mol/l}$	169	1.00 (1.00–1.00)	0.60
Urea, mmol/l	167	1.02 (1.00–1.04)	0.10
Albumin, g/l	93	0.98 (0.95–1.02)	0.34
Diabetes mellitus	168	1.05 (0.66–1.66)	0.84
Ischemic heart disease	168	1.48 (0.95–2.31)	0.09
Peripheral arterial disease	168	1.26 (0.65–2.45)	0.50
Active or past malignancy	164	0.67 (0.38–1.18)	0.17
Being seen by a nephrologist	156	0.49 (0.31–0.75)	0.001
Starting with an AV fistula	167	0.42 (0.24–0.74)	0.002
AV fistula at any time ^b	167	0.52 (0.33–0.82)	0.005
Starting in hospital setting	158	3.29 (1.33–8.16)	0.01
Living at home	153	0.66 (0.35–1.25)	0.20

^a One patient died on the day of the first dialysis and is excluded from all Cox analyses.

^b As segmented time-dependent covariate using the last known AVF status.

Fig. 1. Kaplan-Meier survival analysis.

an AVF and presence of AVF at any time (as a segmented time-dependent covariate, using the last known AVF status) were significant predictors of better survival (table 4). All predictors were tested for proportionality of the hazards by testing for interaction between an independent variable and natural logarithm of time; none of the inter-

Table 5. Results of multivariate Cox regression analysis including all predictor variables which were significant in the univariate models (n = 118)

Parameter	Hazard ratio (95% CI)	p value
Age	1.10 (1.01–1.20)	0.02
Phosphate	1.29 (0.84–1.97)	0.25
Being seen by a nephrologist	0.48 (0.28–0.82)	0.006
AV fistula at any time ^a	0.62 (0.34–1.14)	0.12
Starting HD in-hospital	1.80 (0.68–4.76)	0.24

^a As segmented time-dependent covariate.

actions were significant. When significant predictors from univariate models were included in a multivariate Cox regression analysis in addition to age only being seen by a nephrologist remained an independent predictor (table 5).

Discussion

Our analysis of a subset of a national cohort showed a good survival of very old incident hemodialysis patients, but was unable to identify other predictors of survival in addition to age and prior nephrology care. Additionally, this study provides observational data on the circumstances of dialysis initiation as well as dialysis prescription in this growing population. We have already reported on increasing of the median age of incident renal replacement therapy patients in the past years in our registry [2] and the proportion of very elderly is indeed high, reaching 1 out of 8 patients initiating dialysis during the observed period in the current study.

Our study only included patients who started with dialysis, so there was no control group. The observed overall survival was relatively good (a median of a little more than 2 years), although much shorter than median life expectancy of the general population at this advanced age (i.e. 7.3 years). It should be noted that, overall, dialysis was initiated relatively late (mean eGFR of 7 ml/min/1.73 m²). Similarly good survival was reported also from other centers in Europe [9], including those with a formally established maximum conservative management program [10, 11], while lower survival rates are reported in the USA [12], which is also the case for the general dialysis population [13]. Although no survival benefit of dialysis versus conservative treatment in the very elderly was re-

ported in some studies [14], especially in the setting of high comorbidity [15], there are many reports on a clear survival benefit [10, 16, 17]. Nevertheless, initiation of dialysis does have some negative impact on the quality of life [17] and was even declared ‘dangerous’ [18]. The question of a meaningful prolongation of survival with dialysis in very elderly patients is of course dependent on the starting point of observation and if this is set too early (e.g. when eGFR drops below 15 ml/min/1.73 m² [14, 15]) the survival benefit might be ‘diluted’ or even lost, since mortality is high at that age. In spite of some concerns about the quality of this prolongation of life in light of a decline in functional status associated with the initiation of dialysis [19], we believe that in general it is sufficient to justify the initiation of maintenance dialysis.

We do not know a lot about the circumstances in which this growing population of elderly patients is starting dialysis [9, 11]. As expected, comorbidities are common but our data also shows that the presence of malignancy was also not rare, but in spite of that, the vast majority of the patients were living at home when initiating dialysis. Hemodialysis was initiated relatively late (mean eGFR of 7 ml/min/1.73 m² and mean creatinine of 672 µmol/l), which is probably the result of postponing dialysis until it became absolutely necessary, a policy often applied in this frail population. Studies have shown no benefit of early initiation of dialysis in the elderly [20, 21]. In spite of late initiation mean laboratory results before initiation, including potassium, phosphate, hemoglobin and albumin were acceptable and (except for hyperphosphatemia) within target range and therefore do not suggest an overlooked uremia.

Almost two thirds of patients were seen by a nephrologist in the 3 months preceding initiation of dialysis, nonetheless the great majority started dialysis with a catheter and in the hospital setting, none of which is desired as a standard of care. The patients with at least some prior nephrology care had a significantly higher probability of starting dialysis with an AVF and in an outpatient setting, although the latter was rare anyhow, and pre-dialysis nephrology care was also the only independent predictor of survival in multivariate model in addition to age. It is conceivable that acute illness requiring hospitalization often resulted in worsening of the renal function and initiation of dialysis, which resulted in a high incidence of in-hospital initiations. In-hospital initiation of dialysis can also be more convenient for the nephrologist, since this is an old and frail population, sometimes also lacking social support. Therefore it is also possible that patients with advanced kidney disease and

an imminent need for dialysis were hospitalized to facilitate the initiation of dialysis.

There is a clear survival benefit of patients having an AVF as compared to a catheter in the general dialysis population [22]. AVF at dialysis initiation was predictor of better survival also in our univariate analysis, but when used as a time-dependent predictor in multivariate analysis (we had information on vascular access at two different time points) it was no longer significant. In the elderly patients with chronic kidney disease the risk of dying can be greater than the risk of starting dialysis and therefore a significant proportion of AVFs constructed never get used due to prior death of the patient [23]. The timing of AVF placement in the elderly should therefore be carefully chosen. A relatively small proportion of our cohort (22%) started dialysis with an AVF, but the percentage increased during the first year on hemodialysis to almost 50%; the patients with prior nephrology care had a higher prevalence of AVFs. This low prevalence of AVFs at initiation of dialysis, combined with our previous report of a high likelihood (84%) of constructing an AVF also in elderly patients referred for vascular mapping [24] probably means that our patients were nevertheless not referred for mapping frequently enough, and this is an area of opportunity for improvement. The DOPPS study, on the other hand, reports a very high prevalence of AVFs (70–80%) also in the elderly patient groups [25].

Data on prescription of dialysis in the elderly is also quite rare [25], since this is not commonly recorded in the registries. The prescription of dialysis in our cohort shows a trend of reducing the burden of treatment by reducing the weekly number of sessions in many patients and weekly duration of dialysis sessions resembles that. One third of patients were also dialyzed in single-needle mode, much more than what we have reported for the whole di-

alysis population in the last registry report [2], which probably correlates with a significant use of catheters in the elderly. It is a limitation of this study that we do not have data regarding dialysis efficiency, which would show if this reduction of dialysis dose is appropriate. The use of epoetins was comparable to the general dialysis population [2], so there was no rationing in the treatment of anemia.

To conclude, although almost two thirds of very elderly patients had some prior nephrology care, the great majority nevertheless started dialysis with a catheter and in hospital setting. Data regarding prescription of dialysis shows a trend of reducing the burden of treatment by reducing weekly duration of dialysis. We estimate the observed median survival of a little more than 2 years as good and worthy of initiating dialysis at this advanced age, also due to the absence of strong predictors of outcome, pertaining to the patient. In a multivariate model, only age and prior nephrology care were independent predictors of survival.

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Disclosure Statement

The authors have no conflicts of interest to disclose.

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