ORIGINAL ARTICLE

Port J Nephrol Hypert 2017; 31(4): 268-273 • Advance Access publication 11 December 2017

Predicting early mortality in incident hemodialysis patients: strengthening a shared decision-making process

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Received for publication: Oct 2, 2017
Accepted in revised form: Nov 15, 2017

ABSTRACT

Introduction: The benefits of dialysis in the elderly are dubious. A shared decision-making process, helped by adequate prognostic tools, is essential to determine which patients are better candidates for conservative care. Based on a recent USRDS validated score, this study aimed to identify risk factors associated with early mortality (first 90 days) in a Portuguese cohort of patients.

Methods: A total of 197 patients who initiated hemodialysis treatments in a Portuguese facility between 2005 and 2015 were included. Clinical and laboratory data were collected at time of admission to center. Multiple regression models were performed and fitted to identify potential predictors of early mortality.

Findings: Total of 93 (47.2%) deaths with 23 (11.7%) deaths occurring in first year. In the first three months, there were 15 (7.6%) deaths. Of those who died in first three months, most were men (n=10; 5.1%), mean age 73.5 ± 6.82 years. Almost half (n=7; 3.6%) were dependent and the majority (n=12; 6.1%) had history of hospitalizations in previous year before admission. They had a higher prevalence of hypoalbuminemia and cardiovascular risk factors. Mortality associated factors were albumin level low (<3.5 g/dL) or unknown (OR 5.73; p<0.05), ischemic cardiomyopathy (OR 4; p<0.05) and history of hospitalizations in previous year before admission (OR 4.3; p<0.05). Absence of history hypertension was associated with a reduction of risk (OR 0, 18, p<0.05).

Discussion: Some elements of USRDS score were associated with greater risk for early mortality in this Portuguese cohort of patients. Further investigations are needed in order to validate a specific prognostic tool in Europeans.

Keywords: elderly, conservative care, mortality risk factors, prognostic tools

INTRODUCTION

Chronic kidney disease already affects 10% of the population worldwide. Prevalence can vary from 11.8% in United States to 17.3% and 18.3% in Europe and China, respectively[1].

Numbers are expected to increase disproportionally in countries where the percentage of elderly people is growing[1-4]. Older patients (≥ 65 years) are the fastest-growing segment of the incident end-stage renal disease (ESRD) population and have nearly doubled since 1997[3]. A 57% age-adjusted increase in dialysis for octogenarians and nonagenarians was documented in the United States between 1996 and 2003[5,6]. Currently, more than half of patients initiating dialysis are > 60 years of age[6]. However, evidence from the last decade has revealed that overall benefit of dialysis in these age segments is dubious and may be detrimental to survival and quality of life[6,7].

Nephrologists around the world face the challenge of determining which patients are more appropriate for conservative management as an alternative to dialysis, raising multiple moral and ethical questions.

The Renal Physician Association guideline on appropriate initiation and withdrawal of dialysis recommend an estimation of survival chances for all patients requiring dialysis. Numerous scores for mortality prediction have been developed in last decade but only a few of them have focused on short-term survival (≤ 6 months). The French REIN registry[8] and the New England HD clinics score[9] are robust and proper validated tools for 6-month survival estimates[10].

Recently, Thamer and his colleagues validated a simple 3-month survival score after dialysis start using the US Renal Data System, which considered data from 69,441 patients with age ≥ 67 years[11]. It uses routinely and readily available information that can be used by patients, families and their nephrologists to estimate the risk of early mortality after starting dialysis. In comparative analysis to UK and French models, it has been shown to have the best model fit and discrimination capacity[11].

Considering this study, we aimed to investigate early mortality risk factors in a Portuguese cohort of hemodialysis patients.

MATERIALS AND METHODS

Study population, Setting, and Design

Data from all patients who initiated hemodialysis (HD) treatments in a Portuguese facility between January 2005 and December 2015 were collected using the facility system. Sociodemographic data, comorbid information and medical history, health resource use, institutionalization, dialysis-related information and laboratory data were retrieved for each patient at time of center admission.

Specifically, 273 patients initiated hemodialysis treatments in this center. Of these, 76 patients were excluded because of missing information. A total of 197 patients were included. The possible dialysis modalities were high flux hemodialysis, hemodiafiltration and nocturnal hemodialysis.

End-points and Risk-Factor Predictors

Primary goal was to analyze all-cause mortality within the first 3 months, since there is a known mortality peak in this period, especially in elderly and severe ill patients[5-9]. Mortality within first 6 months was not selected as end-point since there were only four deaths in this period.

Variables chosen as potential predictors of early mortality were based on the Thamer study (Table 1) and were age, gender, history of hypertension, cerebrovascular disease, ischemic cardiopathy, heart failure, diabetes mellitus, cancer, albumin level low (<3.5 g/dL) or unknown, assistance in daily living activities, residence in nursing home and history of hospitalization more than one time or more than a month in the previous year before center admission.

Table 1

Sample Risk Assessment Questionnaire for Clinician and Patient Use for Those Who Initiate Dialysis, by Thamer et al.[11]

Patient´s Condition	Score if yes
Age category	
< 70 y	1
70 – 74 y	1
75 – 79 y	1
80 – 84 y	2
85 – 89 y	3
≥ 90 y	
Albumin level low (< 3.5 g/dL) or unknown?	1
Needs assistance in daily living?	1
Lives in nursing home?	1
Had or has cancer?	1
Had or has heart failure?	1
Hospitalized > 1x or > 1 month in last year?	1

Statistical Analysis

Baseline characteristics were analyzed by standard descriptive statistics. The Kolmogorov-Smirnov test was used to test normality distribution of variables. Patients were divided into two cohorts: those who died within 3 months after starting dialysis and those who didn´t. A simple comparison was made with respective US Renal Data System cohorts. Posteriorly, a univariate analysis was made. The variables considered were included as possible 3-month mortality predictors in multiple logistic regression with backward elimination method used to define the final risk predictors. We also applied the Sample Risk Assessment Chart used by Thamer et al.[11] to examine the proportions of patients and deaths by score categories (Table 2).

Table 2

Sample Risk Assessment Chart for Clinician and Patient Use for Those Who Initiate Dialysis, by Thamer et al.[11]

Score	Estimated Probability of Dying		
	Within 3 months	Within 6 months	Proportion of Patients With Same Score
0	2%	4%	2%
1	3%	7%	12%
2	7%	12%	25%
3	12%	20%	27%
4	17%	27%	19%
5	22%	35%	10%
6	28%	44%	4%
7	34%	49%	1%
≥8	39%	55%	0,2%

Table 3

Characteristics of patients

Characteristic	n; %
Female Sex	85 (43.1%)
Fistula as the access at first dialysis	135 (68.5%)
Hypertension	161 (81.7%)
Ischemic Cardiomyopathy	51 (25.9%)
Congestive Heart Failure	51 (26.4%)
Cerebrovascular Disease	32 (16.2%)
Diabetes mellitus	79 (40.1%)
Cancer	30 (15.2%)
Albumin level low (< 3.5 g/dL) or unknown	58 (29.4%)
Needs assistance in daily living activities	48 (24.3%)
Living in nursing home	9 (4.6%)
Hospitalized > 1x or > 1 month in last year	71 (36%)

RESULTS

Median age was 71 ± 15.5 years. Patient characteristics are summarized in table 3. In total, there were 93 (47.2%) deaths. Only 23 (11.7%) of them occurred in the first year. The first three months was the period with a higher density of deaths (n=15; 7.6%).

A comparison with USRDS cohort is made in table 4. Between two groups, major differences were in the higher prevalence of central venous catheter as first vascular access, diabetes mellitus, ischemic cardiomyopathy, hospitalizations and institutionalization in those who died within 3 months.

In US Renal Data System groups, patient characteristics were similar, except in institutionalization rates and first vascular access, with catheter also being more frequent in those who died within 3 months.

After applying the Sample Risk Assessment Chart (table 5), a great majority of patients were categorized between

Table 4

Characteristics of patients by mortality status: comparison with US Renal Data System development cohort

Characteristic	Portuguese Cohort		US Renal Data System Cohort	
	Did Not Die within 3 Months (n=182)	Died Within 3 Months (n=15)	Did Not Die within 3 Months (n=46.319)	Died Within 3 Months (n=6.477)
Median Age	71.8 ± 13,49 [64 – 81]	73.5 ± 6,8 [70 -78]	76.7 ± 6,5 [71- 81]	78.7 ± 6.7 [73 – 84]
Female Sex	45. 1%	33. 3%	46.4%	44.5%
Fistula as the access at first dialysis	69. 2%	40%	41.9%	21.9%
Hypertension	80.2%	66.7%	–	–
Ischemic Cardiomyopathy	22%	60%	50.6%	59.2%
Congestive Heart Failure	29.7%	40%	50.8%	64.4%
Cerebrovascular Disease	17.6%	20%	16.5%	19.9%
Diabetes mellitus	38.5%	66.7%	58.8%	55.7%
Cancer	17.6%	13.3%	13.3%	19.5%
Albumin level low (<3.5 g/dL) or unknown	3.64 ± 0.56 [3.4 – 4]	3.19 ± 0.47 [2.9 – 3.4]	3.2 ± 0.65 [2.8 – 3.6]	2.9 ± 0.66 [2.5 – 3.4]
Needs assistance in daily living activities	26.4%	46.7%	19.2%	34.3%
Living in nursing home	4.9%	13.3%	10.4%	24.4%
Hospitalized >1x or > 1 month in last year	35.1%	80%	–	–

Table 5

Sample Risk Assessment Chart by Thamer et al.[11] applied to study population and proportion of deaths within 3 months according to categories

Total Score	Proportion of Patients With Same Score	Estimated Probability of Dying	Deaths within 3 months (n=15)
0	18.8%	2%	0
1	15.7%	3%	1
2	22.8%	7%	2
3	21.8%	12%	5
4	13.2%	17%	6
5	4.1%	22%	0
6	3.6%	28%	1
7	0	34%	0
≥8	0	39%	0

categories 0 and 4, corresponding to an estimated probability of dying at 3 months of 2% and 7%, respectively. The predominance was for categories 2 (22. 8%) and 3 (21. 8%), corresponding to a low/intermediate risk of dying. However, most of deaths in the first 3 months (n=13; 6.6%) occurred in patients categorized as 3 and/or 4.

Risk factors for mortality

Table 6 shows the multiple regression analysis. All variables of the simple model had p< 0.05. The absence of hypertension was associated with a reduction of risk (OR 0.18, p<0. 05).

The variables associated with greater risk of global mortality were albumin level low (<3.5 g/dL) or unknown (OR 5.73; p<0.05), ischemic cardiomyopathy (OR 4; p<0.05) and history of hospitalizations in previous year before admission (OR 4.3; p<0.05). Absence of history of hypertension was associated with a reduction of risk (OR 0, 18, p<0.05).

DISCUSSION

International data shows high mortality in elderly patients starting dialysis, with highest rates in the United States and Australia/New Zealand[13]. Causes are multifactorial and related to policies accepting polymorbid and/or advanced age and dependent patients. Some of these patients had experienced renal failure secondary to a systemic illness were already in an active dying process in which dialysis may not alter the course[12,13].

Further to this, there are more debilitating symptoms and geriatric syndromes such as cognitive dysfunction or sensory impairments as well as functional and psychological dependence. Dialysis can impose additional burdens, including invasive procedures. Rehabilitation does not lead to great results and prognosis is generally poor[9-13]. In one study, 63% of patients who decided to initiate dialysis therapy regretted this choice; 52% indicated they initiated therapy by physician´s recommendation[12]. Only 39% of 3702 nursing home ESRD patients with functional impairment maintained baseline function at 3 months after dialysis initiation, decreasing to 13% at 3 months[14].

Many older patients on maintenance dialysis in the United States continue to receive intensive care focused

Table 6

Multiple Regression Models

Variable	Model with all variables (Odd ratio; CI)	Simple Model (Odd ratio; CI)
Age (by year)	0.38 (0.08 – 1.74)	–
Male Gender	1.02 (0.96 – 1.10)	–
Fistula as the access at first dialysis	1.14 (0.26 – 4.63)	–
Hypertension	0.23 (0.04 – 1.20)	0.18 (0.04 – 0.77)
Ischemic Cardiomyopathy	8.68 (1.99 – 46.40)	4.04 (1.13 – 16.1)
Congestive Heart Failure	0.53 (0.12 – 2.06)	–
Cerebrovascular Disease	0.60 (0.09 – 3.09)	–
Diabetes mellitus	1.89 (0.44 – 9.07)	–
Cancer	0.51 (0.05 – 3.02)	–
Albumin level low (<3.5 g/dL) or unknown	0.34 (0.12 – 0.97)	5.73 (1.64 – 24.17)
Needs assistance in daily living activities	1.17 (0.23 – 5.25)	–
Living in nursing home	2.17 (0.09 – 24.61)	–
Hospitalized >1x or > 1 month in last year	4.71(1.10 – 26.38)	4.30 (1.11 – 21.53)

on life prolongation instead of decreasing pain and suffering. About 45% die in hospital setting compared with 35% of patients with other chronic diseases, such as congestive heart failure, dementia or advanced liver disease. During the final month, rates of hospitalization (76%) and intensive care unit admission (49%) are higher than reported for cancer patients[15,16]. However, services of palliative care are extremely low, about 20%, compared with terminal cancer (55%) and heart failure (39%) patients[16-18]. Only 18% expressed preference to live as long as possible, independent of suffering[19]. Similarly, in Canada, only 18% favored dialysis to prolong their lives and there were more patients wishing to die at home (36%) or in an inpatient hospice (29%) than in a hospital (27%)[20]. Also, dialysis represents one of the most expensive public-financed treatments, costing billions per year. Appropriate resource allocation is fundamental[21].

Taking all this into account, it's fundamental to identify who benefits from dialysis, when to start dialysis and what the ideal modality is. This is now instituted as a priority in developed countries[22-25].

Before the release of the IDEAL trial[23], elderly were starting dialysis at higher GFRs. It has been suggested that the severity of renal disease may be overdiagnosed based on method inaccuracies and the elderly probably have slower progression to ESRD, being most likely to die than progress to ESRD. Conservative (nondialytic) care is widely provided but, until recently, it has not been clearly defined and multiple alternative terms have been applied, preventing adequate studies in this field[23]. The recent KDIGO conference on supportive care in chronic kidney disease[24] proposed the term "comprehensive conservative care", a holistic approach patient-centered, focused on patient goals, relief of suffering, preservation of functional status and quality of life[12,22]. The shared-decision making process assumes a central role, in which clinicians, patients and families join together to consider the best medical evidence in light of patient's characteristics and values when choosing health care[26].

Evidence on conservative care is limited but it's reasonably clear that dialysis is associated with a significant survival advantage but it's markedly reduced for older (> 75 years) and polymorbid patients (especially ischemic cardiomyopathy) or with poor functional status. Quality of life, symptoms and hospital-free survival must be considered[22].

Information about patients on peritoneal dialysis (PD) is scarce. PD patients are younger, fitter and more independent so comparisons are difficult. Also, the elderly that are more severe ill and dependent are more likely to receive HD as a most suitable modality[27]. Further studies are needed to clarify the contribution of each dialysis modality into prognosis.

The patient-specific estimate of prognosis is recommended to facilitate informant consent and to support the discussion of care goals[23,24]. Numerous scores of mortality on dialysis have been developed over the course of the last decade,. Scores are integrated prognostic scoring systems that include clinical, biological and other characteristics which when applied to risk estimation are designated as prognostic tools[24]. Although they are not sensitive or specific to predict with certainty how well a patient will do or how long he/she will live, they help to identify high-risk patients who can be targeted for specific interventions or alternative care pathways.

However, the process of score creation is hard and complex, due to the multiple comorbidities and overlap diagnoses. A recent national study in Canada[26] revealed that more than 80% of nephrologists were not satisfied with their capacity to predict clinical trajectories.

Current tools validated to predict short-term mortality are the US Renal Data System score, the French REIN registry score, the Catalan renal registry score and the New England HD clinic score[22].

The US Renal Data System score, by Thamer et al.[11], is the largest study that included more variables on functional status and dependence. It is addressed to patients, clinicians and society and has a good calibration and discrimination parameters. As far as we know, this is the first non-American study seeking to reproduce similar results in order to establish foundations for posterior investigation and validation in Europe.

Our study was limited by the small sample size and by having few mortality events in the considered time. This is the probable reason why further risk associations with the other elements of USRDS score were not found.

The retrospective design limits the accuracy in data collection and correction for residual confounders. Also, there were no specific inclusion criteria other than the beginning of hemodialysis treatments in this facility. We didn´t take into consideration the effect of different dialysis modalities in survival rates. Nocturnal dialysis was a recent option and hemodiafiltration was not always available.

However, we were able to confirm the importance of functional status and recent hospitalizations, as a marker of frailty, in mortality and prognosis. We identified a new element, no history of hypertension, as a positive prognostic marker. Hypertension is intimately linked to cardiovascular disease and cardiomyopathy and cardiovascular diseases are the main cause of death in these patients, so no past history of hypertension may be an indicator of significantly less severe disease and as a consequence of that, better outcome.

CONCLUSIONS

The elderly is the fastest growing segment of incident and prevalent patients on dialysis. They have more disability, symptom burden and comorbidities and their quality of life and prognosis are poorer. Conservative care programs have shown benefits and have to be adequately explored in the right patients, through a shared decision-making process, for which prognostic tools are fundamental. There are several validated scores and the US Renal Data System score is a good candidate with focus on disability and functional status. It seems that some of the elements of this score are suitable for European patients, but further investigations are needed in order to design and validate a specific prognostic tool.

Disclosure of potential conflicts of interest: none declared

ACKNOWLEDGMENTS

We thank Thamer and colleagues for permission to use material from their work in our study. All authors played a part in the drafting of the manuscript, search strategy, data extraction and results' interpretation and discussion. All contributed with medical expertise on hemodialysis and on methodology. CB performed the bibliographic research and wrote the manuscript. CS performed the statistical analysis.

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