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First year survival of patients on maintenance dialysis treatment in Poland

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ABSTRACT

Retrospective analysis of demographic and clinical data of all patients starting dialysis over two years in our Department (n = 105) has been conducted. Factors such as type of dialysis treatment, reason of end-stage renal disease, Body Mass Index (BMI), laboratory tests results, number and cause of death during first year of dialysis were taken under consideration. Five patients have been excluded from the analysis of mortality (four received renal transplantation, one changed dialysis center). Twenty tree deaths have been noted during first year of dialysis treatment. Nine of them occurred during the first three months of therapy. The leading cause of death was cardio-vascular events (n = 14, 60.9%), the second was malignancy (8, 34,8%), one patient died due to catheter associated infection. Malignancy as a cause of end-stage renal disease, lack of outpatient nephrology care, acute mode of beginning renal replacement therapy and lack of erythropoiesis stimulating agents therapy were associated with higher risk of all-cause mortality during first year of dialysis. Being under the outpatient nephrology care, etiology of ESRD other than malignancy and erythropoiesis stimulating agents therapy were independently associated with better survival during this period of time. Other independent variables did not reach statistical significance. To conclude, in order to improve one year survival of dialysis patients, outpatient nephrology care with adequate amount of visits and associated dialysis therapy should be employed.

Key Words: end-stage renal disease, dialysis, mortality, risk factors.

INTRODUCTION

End-stage renal disease (ESRD) is a still emerging medical and socio-economical problem.[1)] Renal replacement therapy is used among two million people all over the world.[1)] The number of patients requiring this type of treatment increases each year. In Poland, as in other developed countries annual accretion was 4.7–3.7% in 2011–2012.[2)] Despite the progress in the availability of renal replacement therapy mortality is still high in this group of patients. First year mortality is the highest and reaches levels of 15–25% in other countries.[3)] Nowadays most hemodialysis patients are 65–74 years old and the main causes of renal disease are: diabetic nephropathy, primary glomerulonephritis, hypertension nephropathy and polycystic kidney disease.[4)] The main causes of death are cardiovascular diseases, infections and malignancy.[3)]

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The aim of the study was to identify the main causes of death and the risk factors of increased mortality during the first year of renal replacement therapy in Poland. Poland doesn't have a center registry of dialysis patients. We present experiences from one dialysis center in Warsaw.

METHODS

Retrospective analysis of demographic and clinical data of all patients starting renal replacement therapy between January 2010 and December 2012 in the Military Institute of Medicine, Warsaw (Poland) has been done. The following data was collected: type of dialysis therapy, reason of end-stage renal disease, type of vascular access, being under the outpatient nephrology care, mode of beginning dialysis treatment, Body Mass Index (BMI), total protein, albumin, cholesterol, hemoglobin concentrations at the moment of beginning dialysis, erythropoiesis stimulating agents therapy and number and cause of death during the first year of dialysis therapy.

Statistical analysis has been done using the Cox proportional hazards model. Transfers to renal transplantation were treated as censored observations. P value less than 0.05 was considered statistically significant. All analysis was performed using SPSS software v.18.0.

RESULTS

We included 105 patients (36 female, 69 male), age 61.74 ± 16.04. Characteristic group is presented in table 1. All patients in the study were Caucasians. Most patients were treated with

Table 1 Characteristic of the population. (N=105)

Age	61.74 SD 14.04	–
BMI	24.96 SD 5.09	–
Gender (Male : Female)	69 : 36	65.7% : 34.3%
Type of dialysis		
Peritoneal Dialysis		19 person 18%
Hemodialysis		86 person 82%
Reason of ESRD		
Diabetes mellitus		21 person 20%
Primary glomerulonephritis		24 person 22.9%
Arterial hypertension		17 person 16.2%
Heart renal syndrome type 2		6 person 5.7%
Vasculities		7 person 6.7%
Malignancy		8 person 7.7%
PCKD		7 person 6.7%
Others		15 person 14.2%
Type of dialysis begun.		
Planned		57 person 54.4%
Acute		48 person 45.7%
Ambulatory nephrology care before the beginning of dialysis.		
Yes		71 person 67.6%
No		34 person 32.4%

PCKD – polycystic kidney disease

hemodialysis (86, 81.9%). The most common reason of end stage renal disease was primary glomerulonephritis (24, 22.9%) followed by diabetic nephropathy (21, 20.0%), hypertensive and atherothrombotic nephropathy (17, 16.2%), malignancy (8, 7.6%), polycystic kidney disease (7, 6.7%), secondary glomerulonephritis (7, 6.7%), cardio-renal syndrome type II (6, 5.7%) and others (15, 14.3%).

Most patients began dialysis in a planned manner (57, 54.3%). Among hemodialysis patients the most common vascular access was catheter (64, 74.4%), the rest of these patients were treated using arteriovenous fistulas (n=22, 25.6%). Catheterization techniques are listed in table 2. Seventy one patients were under outpatient nephrology care before dialysis therapy (67.6%). Among them only 19,7 % started dialysis treatment in an acute manner.

Mean BMI was 24.79 ± 5.10 kg/m^2. Median protein concentration was 6.1 ± 1.0 g/dl. Forty three patients (47.8%) had total protein concentration lower than 6.2 g/dl. Mean albumin concentration was 3.44 ± 0.73 g/dl. Forty six patients (48.4%) had serum albumin concentration lower than 3.5 g/dl. Mean serum cholesterol was 172 ± 58 mg/dl. Sixty three individuals (72.4%) had serum cholesterol lower than 200 mg/dl. Mean hemoglobin concentration was 9.5 ±

Table 2 Associations between selected characteristics and mortality risk during the first year of dialysis treatment.

Independent variables		Deaths n(%)	HR	Cox regression* 95% CI	p
BMI (N=100)	<18,5	2 (50%)	2,481	0,547–11,246	0,351
	18,5–24,9	13 (22,8%)	ref.	–	
	25,0–29,9	4 (15,4%)	0,683	0,223–2,099	
	>=30	4 (30,8%)	1,806	0,578–5,635	
Type of dialysis (N=100)	HD	20 (23,8%)	1,12	0,325–3,877	0,856
	CAPD	3 (18,8%)	ref.	–	
Dialysis acces (N=100)	A-V fistula	1 (4,5%)	ref.	–	0,188
	Tenckhoff catheter	2 (15,4%)	4,169	0.372–46.722	
	Cuffed catheter	11 (30,6%)	5,713	0,734–44,489	
	Non-cuffed catheter	9 (31,0%)	8,85	1,111–70,521	
Etiology of ESRD (N=100)	Diabetic nephropathy	3 (15,0%)	0,163	0,038–0,69	0,033
	PG, SG, PKD, others	10 (20,4%)	0,285	0,095–0,853	
	Cardio-renal syndrome+HT	5 (21,7%)	0,202	0,057–0,714	
	Malignancy	5 (62,5%)	ref.	–	
Outpatient care (N=100)	yes	9 (13,6%)	ref.	–	0,012
	no	14 (41,2%)	2,982	1,276–6,964	
Acute start of dialysis (N=100)	yes	15 (32,6%)	2,443	1,035–5,767	0,042
	no	8 (14,8%)	ref.	–	
ESA treatment (N=100)	yes	10 (14,5%)	ref.	–	0,004
	no	13 (41,9%)	3,38	1,468–7,782	
Serum protein (N=82)	<6,2g/dl	9 (21,4%)	1,282	0,494–3,326	0,61
	>=6,2g/dl	8 (20%)	ref.	–	
Serum albumin (N=90)	<3,5g/dl	14 (30,4%)	2,169	0,875–5,377	0,094
	>=3,5g/dl	7 (15,9%)	ref.	–	
Serum hemoglobin (N=95)	<11g/dl	18 (22,8%)	0,918	0,309–2,722	0,877
	>= 11g/dl	4 (25%)	ref.	–	
Serum cholesterol (N=82)	<200mg/dl	10 (16,4%)	ref.	–	0,239
	>=200mg/dl	5 (23,8%)	1,925	0,648–5,724	

Abbreviations: A-V fistula, arterio-venous fistula, BMI, body mass index, CAPD, continuous ambulatory peritoneal dialysis, CI confidence interval, ESA, erythropoiesis stimulating agents, ESRD, end-stage renal disease, HD, hemodialysis, HR, hazard ratio, HT, hypertensive and atherothrombotic nephropathy, PG, primary glomerulonephritis, PKD, polycystic kidney disease, SG, secondary glomerulonephritis.
*) age adjusted

Table 3 Association between etiology of ESRD, being under outpatient nephrology care, erythropoiesis stimulating agents therapy in Cox survival model adjusted for age

Independent variables		HR	95% CI	p
Etiology of ESRD	Diabetic nephropathy	0.276	0.058–1.310	0.016
	PG, SG, PKD, others	0.463	0.139–1.544	
	Cardio-renal syndrome+HT	0.124	0.033–0.459	
	Malignancy	Ref.	–	
Outpatient care	Yes	Ref	–	0.032
	No	2.805	1.090–7.219	
ESA treatment	Yes	Ref	–	0.002
	No	4.335	1.725–10.892	

Abbreviations: CI confidence interval, ESA, erythropoiesis stimulating agents, ESRD, end-stage renal disease, HR, hazard ratio, HT, hypertensive and atherothrombotic nephropathy, PG, primary glomerulonephritis, PKD, polycystic kidney disease, SG, secondary glomerulonephritis

1.7 g/dl. Most patients had hemoglobin concentration under 11 g/dl (84, 84.0%) at the moment of beginning the treatment. As a consequence most patients received erythropoiesis stimulating agents (72, 69.2%) after beginning renal replacement therapy.

Five patients have been excluded from the analysis of mortality, because 4 of them received renal transplantation and one changed dialysis centers and was unavailable to follow-up. Twenty three deaths have been noted during the first year of dialysis treatment. Nine of them occurred during the first three months of therapy. The most common causes of death were cardio-vascular events (n=14, 60.9%) like: myocardial infarctions, strokes and sudden cardiac death. The second leading cause of death was malignancy, (8, 34,8%) most frequently pulmonary cancer and multiple myeloma. One patient died due to catheter associated infection.

After adjusting for age, malignancy as a cause of end stage renal disease, lack of outpatient nephrology care, acute modes of beginning renal replacement therapy and lack of erythropoiesis stimulating agents therapy were associated with higher risk of all-cause mortality during first year after starting dialysis. Other factors like: type of dialysis, BMI, serum protein, albumin, cholesterol and hemoglobin concentrations did not influence survival. Associations between selected characteristics and mortality risk are presented in table 2. Excluding the influence of age, the multivariable Cox's survival model revealed that being under the outpatient nephrology care, the etiology of ESRD other than malignancy and erythropoiesis stimulating agents therapy were independently associated with better survival during first year renal replacement therapy (Table 3).

DISCUSSION

In recent years the population of patients undergoing renal replacement therapy is changing. The mean age of patients beginning dialysis treatment is increasing. In this study the mean age was 61.74 ± 16.04 years. Fifty three percent of patients were above 60 and 31% were above 70 years old.

Nowadays the leading cause of primary renal disease is diabetes mellitus. In the United States, diabetic nephropathy accounts for 45% of end stage renal disease as opposed to Europe where the figure is 20%.[4,5] In this study the most common reason for end stage renal disease was primary glomerulonephritis (22.9%), diabetic nephropathy was second (20.0%). The difference was not significant and incidence of diabetic nephropathy is comparable to other European countries.

Relatively numerous groups of patients with primary glomerulonephritis can be associated with the location of our dialysis center in a multidisciplinary medical institute with a nephrology department.

This fact can also influence the high percentage of patients treated with peritoneal dialysis. In our study 18% of patients were treated with this method. In Poland 6% of patients with end-stage renal disease are treated with peritoneal dialysis, in comparison with 5% in the US and 30% in Germany, Sweden, Spain and Denmark.[2,4,5]

Outpatient nephrology care in the predialysis period is associated with longer patient survival during the first year of dialysis therapy.[6] Nephrologists supervision enables renal replacement therapy among well-prepared patients and in the most appropriate time.[7,8] Our study demonstrates that patients who were not referred to nephrologists before dialysis treatment had almost three times higher risk of death in comparison to patients under nephrologists care. Similar results are described in literature. *Minutolo et al.* observed that lack of nephrology care was associated with increased mortality in patients with chronic kidney disease stage 3b-5.[9]

Unplanned beginning of dialysis in most cases requires usage of catheters (cuffed or non-cuffed) as a vascular access. This situation is associated with lower survival rates in this group of patients. In a large, multicenter study, *Lorenzo et al.* showed that unplanned beginning of dialysis therapy with catheter was associated with increased mortality. During a one year follow-up the amount of deaths in this group was three times higher.[7] Similar results were observed in our study. Unplanned beginning of dialysis treatment was associated with higher risk of death (HR - 2,44) during the first year of therapy. In the presented study relations between dialysis access and mortality did not reach statistical significance, however HR for cuffed (5,71) and non-cuffed catheters (8,85) was high. On the other hand using arterio-venous fistula as a vascular access was associated with the lowest risk of death. This type of vascular access is thought to be the most appropriate, with the lowest risk of infectious complications.[10] Nowadays the amount of older patients, with atherosclerosis, diabetes mellitus is increasing. That is why formation of arterio-venous fistula is very often unsuccessful and impossible. According to American data 1–2% of dialysis patients die because of a lack of dialysis access.[11]

Introduction of erythropoiesis stimulating agents (ESA) was one mile stone in renal replacement therapy. However some observations revealed an association between ESA doses and mortality. *Duong at al.* demonstrated a higher mortality risk in hemodialysis patients with increasing ESA doses and a higher ESA responsiveness index.[12] In our study ESA treatment was associated with lower risk of death in the first year of dialysis treatment. But the first period of ESA treatment is partially a correction phase and usually high doses are not used in this time.

Protein energy wasting is one of the risk factors of increased morbidity and mortality among dialysis patients.[13] This complication concerns 20–70% of hemodialysis patients and 18–50% of patients treated with peritoneal dialysis.[14,15] In the present study some nutritional markers like: BMI, serum protein, serum albumin and serum cholesterol concentrations were chosen to check their association with survival. BMI is known to be a risk factor of mortality. Contrary to the general population of dialysis patients lower BMI is associated with lower chances of survival.[16] However this relation takes a U-turn with the most protective BMI of 30 kg/m^2.[17] In our study the relationship the between BMI and mortality did not reach statistical significance. However low BMI (<18,5) as well as high BMI (>30) were associated with increased mortality in comparison with individuals with BMI between 18,5 to 24,9 kg/m^2. This fact can be explained by the short period of observation (one year) compared to *Huang at als* study of five years.[17]

Our study did not confirm the previous findings that low serum albumin concentration correlates with worse survival.[18] We did not observe statistically significant association between serum albumin concentration and risk of death among dialysis patients (p = 0,094). Other

biochemical markers did not influence patient's survival either. The limitation of the study was that such parameters like body composition with amount of fat tissue mass and lean tissue mass were not taken into account.

According to data from the literature, the highest mortality is observed during the first three months after starting dialysis therapy. In our study nine out of twenty three deaths were noted in this period. Similar to other centers, which show 15–20% one year mortality, we observed 23%.[19] Cardiovascular events were the main cause of death in this study population as well as in other dialysis populations. Cardiovascular events are the leading cause of death amongst first year dialysis patients and after 5 or 10 years.[20,12] Chronic anemia, iron deficiency, insulin resistance and vitamin D deficiency are considered to be the risk factors of cardiovascular complications.[22,23,24]

Contrary to international data, in our study infections were the third reason for death and were preceded by malignant diseases. Low percentage of death because of infections (4.3%) with high prevalence of catheter usage can be associated with early diagnosis and early, proper antibiotic treatment after recognizing the first symptoms.

Relatively high mortality during the first year and the first three months of dialysis treatment can be associated with a severe general state of the patients. Many patients who started dialysis treatment were of an advanced age, began dialysis treatment in an acute manner, had malignancy or did not have a chance for arterio-venous fistula because of the poor state of their vessels.

Outpatient nephrology care with an adequate amount of visits and associated dialysis therapy could probably ameliorate one year survival of dialysis patients.

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