

SURVIVAL OF PATIENTS ON MAINTENANCE HAEMODIALYSIS OVER A TWENTY-YEAR PERIOD

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Abstract: Patient survival is a key index of the overall adequacy of treatment in most chronic diseases. Analyses of survival of patients undergoing haemodialysis is very important, as it may offer clues and ideas for prolonging survival of patients with end-stage renal disease (ESRD). The aims of this study were to describe the characteristics of the patients on maintenance haemodialysis therapy over a period of 20 years, to determine the survival rate of these patients according to ages at the onset of haemodialysis, the primary renal diseases, and the cause of death, and to determine the survival rate at five, ten, fifteen and twenty years of haemodialysis treatment at our centre.

The charts of 518 unselected patients, 282 male and 236 female, treated with maintenance haemodialysis therapy in a period of 20 years (1985–2005) were reviewed. At the time of evaluation, 164 patients were currently being treated, and 354 patients overall had been diseased. Statistical analysis was performed to evaluate the relationship between survival and patient characteristics such as age, gender, primary renal disease, and age at dialysis onset. Actual survival rates were determined by the Kaplan-Meier method.

The survival rate of our patients treated with maintenance haemodialysis was 60% at 5 years, 37% at 10 years, 25% at 15 years and 9% at 20 years. Female patient survival was superior to male. Patients aged under 40 at the start of dialysis had a better survival probability compared to older patients. Patients with diabetes mellitus and nephroangiosclerosis, had a lower survival rate compared to patients with glomerulo-

nephritis and with adult dominant polycystic kidney disease. Cardiac death was the most common cause of death in patients involved in the study. About 52% of the patients died from cardiovascular disease.

Death is the most severe consequence of inadequate dialysis and can be used as an index of the adequacy of the dialysis therapy. Treatment factors that may improve outcomes include an early start of dialysis therapy, a high dose of dialysis (Kt/V over 1.2), correction of anemia, adequate protein and caloric intake, control of calcium and phosphate metabolism, and the use of biocompatible dialyzers.

Key words: End-stage renal disease, haemodialysis, survival.

Introduction

Patients with end-stage renal disease (ESRD) on maintenance haemodialysis (HD) therapy have an exceptionally high mortality rate compared to that of the general population. As with many chronic medical conditions, the life expectancy of patients undergoing therapy for ESRD is markedly reduced. Without renal replacement therapy, however, these patients would live only a few weeks before becoming uremic and dying [1]. Several factors for such a high mortality rate have been identified, including advanced age, cardiovascular disease and infection. Among them, cardiovascular disease remains the leading cause of death. The cause of cardiovascular disease in haemodialysis patients is multifactorial. Traditional risk factors like hypertension, diabetes and disorders of lipid and calcium metabolism are particularly common among haemodialysis patients, but other non-traditional factors such as chronic inflammation and malnutrition may be more important for the excess of cardiovascular disease in this patient group [2].

Patient survival is a key index to the overall adequacy of treatment in most chronic diseases. Analyses of survival of patients undergoing haemodialysis is very important, as it may offer clues and ideas for prolonging the survival of ESRD patients. A good source for survival studies is the data released at regular time intervals through national or international renal data registries, such as the European Dialysis and Transplant Registry [3].

The aims of this study were to describe the characteristics of the patients on maintenance haemodialysis therapy over a period of 20 years, to determine the survival rate of these patients according to age at the onset of haemodialysis, the primary renal diseases and the cause of death, as well as to determine the survival rate at five years of haemodialysis treatment at our centre.

Patients and Methods

The charts of 518 unselected patients, 282 male and 236 female treated with maintenance haemodialysis therapy over a period of 20 years (1985–2005), were reviewed. At the time of evaluation, 164 patients were currently being treated, and 354 patients had been diseased. The mean (\pm SD) age of the patients at the initiation of HD was 51.9 ± 13.9 years. The demographic data on the patients involved in the study are presented in Table 1.

Table 1 – Табела 1

Demographic data of the patients involved in the study
Причини за смртність кај пациентишто од студирајќи

	Number	%
Gender		
Female	236	45,6
Male	282	54,4
Renal disease		
GN	79	15,3
IPN	128	24,7
ADPKD	30	5,8
NAS	77	14,9
DM	96	18,5
unknown	108	20,8
Age at the onset of HD (years)		
< 20	14	2,7
21–30	33	6,4
31–40	60	11,6
41–50	134	25,9
51–60	129	24,9
61–70	118	22,8
> 71	30	5,8

GN: glomerulonephritis

IPN: interstitial pyelonephritis

ADPKD: adult dominant polycystic kidney disease

NAS: nephroarteriosclerosis

DM: diabetes mellitus

All patients received the same treatment. Standard acetate or bicarbonate haemodialysis treatment was offered. The dialysis duration was 12 hours per week. Cellulose membranes of 1.0–1.3 m² were used. Most of the machines were Gambro AK 10 and Gambro AK 100 models (Gambro, Lund, Sweden). The water for the haemodialysis treatment was processed by reverse osmosis. The blood flow rate was 250–280 ml/min, and the dialysate flow rate was 500 ml/min. There was no reuse of dialysers. The Cimino-Brescia arterial-venous

fistula was typically used for permanent vascular access. Only a few patients, less than 3%, had subclavian catheters or arterio-venous grafts. There were no selection criteria for admittance to the haemodialysis treatment. The recommended diet was low salt intake with mean protein intake of approximately 1 g/kg body weight per day. Calcium carbonate was the principal phosphate binding agent used. Anaemia was corrected by blood transfusions until 1997, and thereafter erythropoietin was widely given.

Statistical analysis was performed to evaluate the relationship between survival and patient characteristics such as age, gender, primary renal disease and age at starting dialysis. Actual survival rates were determined by the Kaplan-Meier method. The z-test was used for estimation of mutual differences. The results obtained are presented graphically. We have used ERA/EDTA recommended abbreviations for diagnosis and codes for the causes of death.

Results

The overall cumulative probability of patient survival was 0.89 (12 months), 0.60 (60 months), 0.37 (120 months), 0.25 (180 months), and 0.09 (240 months), respectively. The cumulative survival probabilities of the patients are shown in Fig. 1. Female patient survival was superior to male. The survival probabilities of patients according to gender are presented in Fig. 2. Age at the

Cummulative survival curve of the dialysis patients

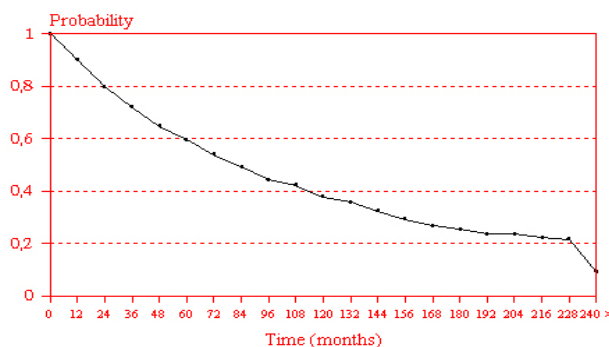


Figure 1 – Cumulative probability of patient survival

Слика 1 – Збирна крива на њреживување

start of dialysis had, as expected, a significant effect on patient survival. Patients aged under 40 at the start of dialysis had a better survival probability compared to the older patients. The worst survival probability was observed in

patients aged over 71 at the initiation of haemodialysis treatment. The cumulative survival probabilities according to the age of the patients at the onset of haemodialysis therapy are presented in Fig. 3. Patients with diabetes mellitus, systemic diseases, nephroarteriosclerosis and interstitial pyelonephritis had a lower survival rate compared to patients with glomerulonephritis and adult

Survival curves of the patients according to gender

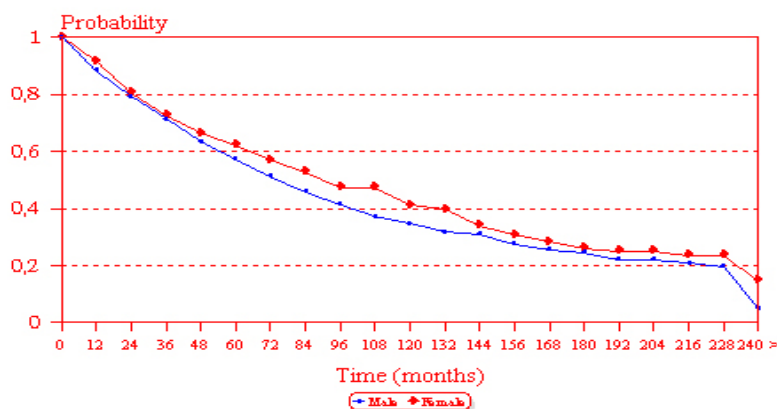


Figure 2 – Probability of patient survival according to gender
Слика 2 – Веројатносии на преживување кај пациентиите во однос на полот

Survival curves of the patients according to age

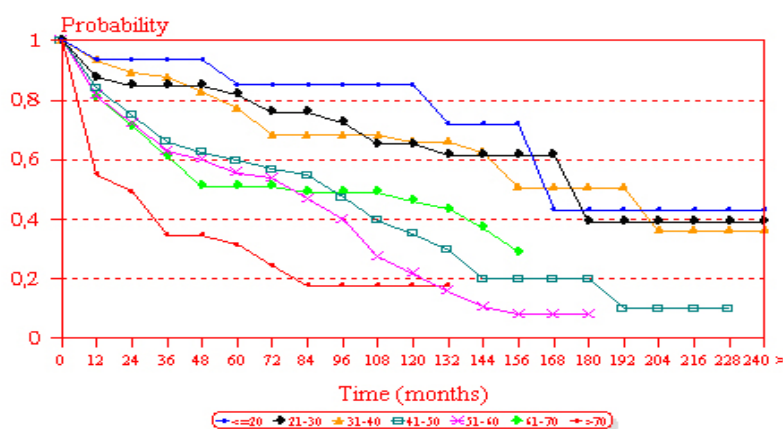


Figure 3 – Probability of patient survival according to age at start

of hemodialysis therapy

Слика 3 – Веројатноста на преживување кај пациентите во однос на возрастта при започнување на лекувањето со хемодијализа

dominant polycystic kidney disease. Diabetic patients had a worse prognosis compared to non-diabetic patients. Fig. 4 shows the probability of survival for patients with primary renal disease. Cardiac death was the most common cause of death in patients involved in the study. About 52% of the patients died from cardiovascular disease. The causes of death in patients are presented in Table 2.

Survival curves of the patients according to primary diagnosis

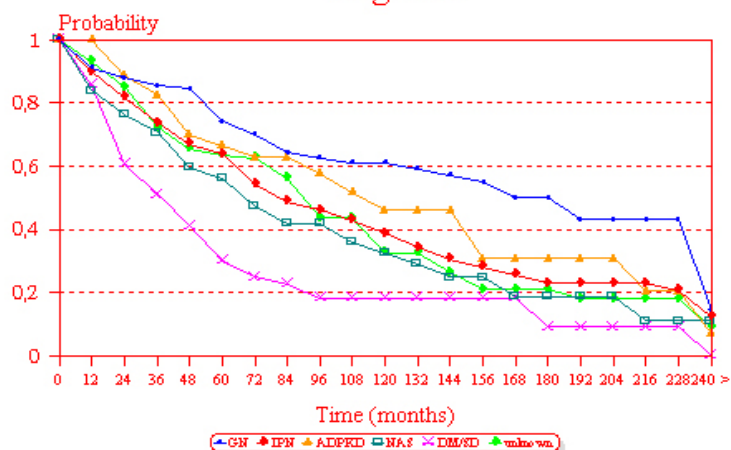


Figure 4 – Probability of patient survival according to primary renal disease

Слика 4 – Веројатноста на преживување во однос на основното ренално заболување

Table 2 – Tabela 2

The causes of death in patients involved in the study

Pri~ini za smrtta kaj pacientite od studijata

Cause of death	Number	%
Cardiac	184	52
Vascular (CVI)	76	21,5
Infection	53	15
Liver disease	16	4,5
Malignancy	14	4
Cachexia	4	1,1

Dementia	4	1,1
Accident	1	0,3
Suicide	2	0,6

Discussion

The survival rate of our patients treated with maintenance haemodialysis was 60 % at 5 years, 37 % at 10 years, 25% at 15 years, and 9% at 20 years. The latest annual report from the ERA-EDTA Registry (2005) showed a patient survival rate of 55.2% at 5 years [3]. Charra *et al.* presented an excellent 20-year survival experience, calculated with 445 haemodialysis patients. Their experience was 87% at 5 years, 75 % at 10 years, 55% at 15 years, and 43% at 20 years [4]. Their arguments for the better survival data than usually reported were the achievement of adequate blood pressure control, adequate protein and energy intake, and a dose of dialysis that was high enough to provide a Kt/V of 1.6.

Some studies have indicated that female patients have a better survival rate than males [5, 6, 7]. This was in agreement with our results, when we compared the survival probabilities of the patients according to gender. Age at the start of dialysis is a significant risk factor for the survival of dialysis patients. The survival rates inversely correlated with the age at the start of dialysis therapy in our study, as well as in the study of Charra *et al.* [4].

One of the major prognostic indicators of early mortality in patients starting dialysis in the study of Gmar-Bouraoui S *et al.* was primary renal disease [8]. They found that diabetes mellitus and amyloidosis were associated with the highest rate of early mortality, 29.7% and 33.3% respectively, and glomerulonephritis and polycystic kidney disease were associated with a low risk of mortality. The same finding was noted in our study and many other series [8, 9, 10, 11]. In the study of Iseki K *et al.*, diabetic patients on dialysis had a significantly worse prognosis when compared to non-diabetic patients (HR: 1.88; 95% CI: 1.55 to 2.28). The probability of survival at 5 years was 0.731 for non diabetic patients and only 0.418 for diabetic patients [12].

Beside the basic factors such as gender, age, and cause of ESRD, co-morbid conditions substantially modify the basal mortality risk. Most patients when starting on dialysis had had renal disease for a variable number of years and presented with anemia, hypertension, salt and water retention, some degree of bone disease and deficiency of vitamin D. One of the most common causes of ESRD was diabetes mellitus, with systemic complications usually quite pronounced by the time ESRD was reached. More co-morbid conditions are expected among patients with diabetic nephropathy than among those with ESRD due to all other causes.

Cardiac disease is the single most important cause of death among haemodialysis patients. The National Institute of Diabetes and Digestive and

Kidney Diseases, in their annual report of 1997, reported a mortality of 44% due to cardiac disease, slightly lower compared to the 52% in our study [13]. Cardiovascular causes accounted for 50% of the reported causes of mortality in dialysis patients and included pericarditis, severe cardiac failure, and myocardial infarction in the study of Gmar-Bouraoui S *et al.* [8]. The most powerful independent predictors of overall morbidity and mortality from cardiac disease in the study of Herzog CA *et al.* were "older age" and "diabetic nephropathy". Their data suggested that dialysis patients who had acute myocardial infarction had high rates of death from cardiac cause and poor long term survival [14].

Survival rates of dialysis patients depend on the dose of dialysis delivered. The HEMO Study was the largest randomized clinical trial designed to determine whether increasing the dose of dialysis would alter survival among HD patients [15]. The conclusion was that patients who were on HD three times per week had no major benefit from a higher dialysis dose than that recommended by the current US guidelines. However, the study conducted by The Japanese Society of Dialysis Therapy reported an improvement in morbidity and mortality at a dialysis dose well above a Kt/V of 1.8, the recommended dose in the current guidelines [16]. Ajiro *et al.* suggested single pool Kt/V of at least 1.28 to improve survival in patients who were on HD for more than 10 years. In the study they evaluated the effect of the dialysis dose in a selected group of patients on long-term HD [2].

The nutritional status of the dialysis patients is also a strong predictor of mortality: undernourished patients had an elevated mortality risk. Greater attention to nutritional therapy might be of benefit to the survival of dialysis patients, since hypoalbuminemia and malnutrition are independent predictors of mortality [17, 18]. In a cross-sectional study of 12000 HD patients, Lowrie *et al.* performed regression analysis to evaluate the association of various laboratory tests with the probability of death. They concluded that a low serum albumin level (< 40 g/l) was strongly associated with the probability of death [19]. Good evidence suggested that restricting dietary protein to less than 1 g/kg body weight was potentially harmful to dialysis patients and that attention to protein and caloric intake was important for generally undernourished patients [20].

Anaemia also plays an important role in the survival of dialysis patients. Several reports from the literature stated that there was an optimal haemoglobin level of 120 g/l to be suggested for dialysis and predialysis patients [21, 22]. However, lower haemoglobin levels were associated with increased mortality [23]. Our previous experience clearly documented the relation between anaemia and left ventricular hypertrophy [24]. We also found that treatment with recombinant human erythropoietin had a beneficial effect on red cell survival in patients with end-stage renal disease [25].

Calcium, phosphate, parathyroid hormone and vitamin D have been shown to be important determinants of survival associated with kidney disease

[26]. Hypercalcaemia and hyperphosphataemia were robust predictors of higher death risk. Serum alkaline phosphatase had an incremental association with mortality [27, 28].

Conclusions

The survival rate of our patients treated by maintenance haemodialysis was 60% at 5 years. More efforts to improve survival are needed, since the relative risk of death is still very high for patients on dialysis. Death is the most severe consequence of inadequate dialysis and can be used as an index of the adequacy of dialysis therapy. Treatment factors that may improve outcomes include the early start of dialysis therapy, a high dose of dialysis (Kt/V over 1.2), adequate protein and caloric intake, correction of anaemia, correction of calcium and phosphorus metabolism, and the use of biocompatible dialyzers.

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Резиме

**ПРЕЖИВУВАЊЕ НА ПАЦИЕНТИТЕ НА ХРОНИЧНА
ХЕМОДИЈАЛИЗА ВО ТЕКОТ НА 20-ГОДИШЕН ПЕРИОД**

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Преживувањето на пациентите претставува основен показател за адекватноста на третманот, речиси, кај сите хронични болести. Анализата за преживувањето на болните лекувани со хронична хемодијализа е многу важна. Таа може да укаже на решенија и да даде идеи за продолжување на преживувањето кај болните со терминална бубрежна слабост. Целта на оваа студија беше да се прикажат карактеристиките на болните лекувани со хронична хемодијализа во текот на 20-годишниот период, како и да се одреди нивното преживување во однос на возраста, полот и примарното бубрежно заболување, а исто така и да се одреди петгодишното, десетгодишното, петнаесетгодишното и дваесетгодишното преживување во нашиот центар.

Анализирани беа историите на 518 болни, 282 мажи и 236 жени, лекувани со хронична хемодијализа во текот на 20-годишниот период (1985–2005). Во моментот на обработката на податоците, активно се лекуваа 164 болни, а 354 пациенти беа починати. Податоците беа статистички обработени, со цел да се утврди корелацијата помеѓу преживувањето и возраста, полот и примарното бубрежно заболување. Кривите на преживување беа пресметувани според методата на Kaplan и Meier.

Преживувањето на пациентите лекувани со хронична хемодијализа изнесуваше: 60% за пет години, 37% за 10 години, 25% за 15 години и 9% за 20 години. Преживувањето на жените беше подолго од мажите. Преживу-

вањето корелираше инверзно со возраста. Пациентите со дијабет, нефро-склероза и системско заболување преживуваа пократко од тие со хроничен гломерулонефрит и адултна полицистична бубрежна болест како примарно бубрежно заболување. Кардијалната причина за смрт, со 52% беше најзаста-пена во однос на сите други причини за смрт кај болните.

Смртта како најсериозна последица на неадекватното лекување би можела да послужи како индекс на адекватноста на дијализната терапија. Факторите кои можат да го подобрат преживувањето се: рано започнување со дијализно лекување, поголема доза на дијализата ($KT/V > 1.2$), корекција на анемијата, адекватен протеински и калориски внес, контрола на метабо-лизмот на калциум и фосфор, употреба на биокompatibilни мембрани.

Клучни зборови: терминална бубрежна слабост, хемодијализа, преживу-вање.

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