

Survival time of patients on hemodialysis. A prospective one-center study

Czas przeżycia pacjentów hemodializowanych. Prospektywne, jednośrodkowe badanie

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Wprowadzenie. Czas przeżycia pacjentów stale hemodializowanych pozostaje na stosunkowo niskim poziomie.

Cel. Analiza czasu przeżycia osób hemodializowanych i jego związku z wybranymi czynnikami socjodemograficznymi i klinicznymi.

Materiał i metody. W badaniu wzięły udział 42 kobiety i 68 mężczyzn (średnia wieku 59 lat; min 24, max 86, Me 59,5). Analizy dokonano przy użyciu modelu proporcjonalnego ryzyka Coxa z oceną ilorazu hazardu (HR).

Wyniki. W badanej grupie 77 pacjentów ze 110 zmarło w czasie obserwacji. Roczne przeżycie chorych hemodializowanych wynosiło 85%, pięcioletnie 41%. W modelu proporcjonalnego ryzyka Coxa, niska śmiertelność była powiązana z obecnością wsparcia ze strony rodziny (HR 0,34; CI 0,18-0,65; $p < 0,002$); podwyższonych wartości BMI (HR 0,91; CI 0,85-0,98; $p < 0,02$) oraz albumin w surowicy (HR 0,35; CI 1,16-0,76; $p < 0,01$). Natomiast podwyższona śmiertelność była powiązana z wiekiem (HR 1,05; CI 1,02-1,08; $p < 0,001$); obecnością chorób sercowo-naczyniowych (HR 2,07; CI 1,05-4,06; $p < 0,05$); podwyższonymi wartościami wapnia w surowicy (HR 1,71; CI 1,34-2,18; $p < 0,001$) oraz fosforanów w surowicy (HR 1,46; CI 1,2-1,78; $p < 0,001$).

Wnioski. Wsparcie rodziny może być czynnikiem istotnie wpływającym na czas przeżycia u pacjentów hemodializowanych i powinno być szeroko brane pod uwagę w opiece zdrowotnej. Wykazano związek wieku, BMI, chorób układu krążenia, stężenia wapnia, fosforanów, albumin z czasem przeżycia osób regularnie hemodializowanych.

Słowa kluczowe: wsparcie rodziny, hemodializa, czas przeżycia, opieka medyczna

Introduction. Survival in patients receiving regular hemodialysis remains relatively low.

Aim. To analyze survival in a group of hemodialyzed patients and its relationship to sociodemographic and clinical factors.

Material & Methods. The study involved 42 women, 68 men (mean age of 59 years; min 24, max 86, Me 59.5). The Cox proportional hazards model with the hazard ratio (HR) estimations were used in this study.

Results. Seventy seven out of 110 patients died during the observation. The 1-year survival of hemodialysis patients was 85%, the 5-year survival was 41%. In the Cox proportional hazard model lower mortality was associated with family support (HR 0.34; CI 0.18-0.65; $p < 0.002$); elevated serum albumin (HR 0.35; CI 1.16-0.76; $p < 0.01$), increased BMI (HR 0.91; CI 0.85-0.98; $p < 0.02$). Higher mortality was associated with age (HR 1.05; CI 1.02-1.08; $p < 0.001$); presence of cardiovascular diseases (HR 2.07; CI 1.05-4.06; $p < 0.05$); elevated serum calcium (HR 1.71; CI 1.34-2.18; $p < 0.001$), serum phosphates (HR 1.46; CI 1.2-1.78; $p < 0.001$).

Conclusion. Family support may be an important factor affecting survival time in patients on hemodialysis and should be widely considered in health care. This study confirmed the association of age, BMI, cardiovascular diseases, serum calcium, phosphates, albumin with survival time of patients receiving regular hemodialysis.

Key words: family support, hemodialysis, survival time, health care

© Hygeia Public Health 2016, 51(2): 209-214

www.h-ph.pl

Nadesłano: 10.10.2015

Zakwalifikowano do druku: 31.05.2016

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Introduction

End-stage renal disease (ESRD) can lead to destruction of all organs, physical and mental activity limitations, disability, and premature death. Survival in ESRD patients is important and widely considered

objectively in medical studies, procedures or services. Hemodialysis is a treatment of unquestionable effectiveness in extending time of survival. However, the hemodialysis treatment and associated medical procedures substantially interfere in all aspects of

the patient's life and survival. In this context, an important issue is to assess factors that are helpful in predicting survival and in building treatment strategies in ESRD patients on hemodialysis. Survival with acceptable health-related quality of life is the most desired goal in the treatment of ESRD patients. In literature it was reported that low albumin and high CRP concentrations along with the use of calcium containing phosphate binders were the strongest predictors of mortality in patients new to hemodialysis [1]. Diabetes is an important risk factor for ESRD. It was also pointed out that the impact of diabetes on survival following ESRD is time-dependent and that differences between genders might exist [2]. Alternatively, some studies found no differences in mortality when comparing patients with and without diabetes [3, 4]. Furthermore, only a few studies conducted survival analyses stratified by gender. In a recent study, a time-dependent effect of diabetes on mortality in patients with ESRD was found, but only in women [5].

Many additional factors were mentioned to be correlated with mortality in dialysis patients [6]. The DOPPS study showed that the crude 1-year mortality rates were 6.6% in Japan, 15.6% in Europe, and 21.7% in the US. After adjusting for age, gender, race, and 25 comorbid diseases, the relative risk (RR) of mortality was 2.84 ($p < 0.0001$) for Europe compared with Japan (reference group) and was 3.78 ($p < 0.0001$) for the US compared with Japan. The adjusted RR of mortality for the US versus Europe was 1.33 ($p < 0.0001$). For most comorbid diseases, the prevalence was the highest in the US, where the mean age (60.5 ± 15.5 yrs) was also the highest. Older age and comorbidities were associated with an increased risk of death (except for hypertension, which carried a multivariate RR of mortality of 0.74; $p < 0.0001$) [7].

Associations between indicators of social support and survival have also been demonstrated in studies of patients with ESRD. McClellan and al. showed in a prospective study that quality of life measures, which included social support, predicted survival of HD patients [8]. Christensen et al. showed that family cohesion, as a social support indicator, was significantly associated with survival, independent of age [9]. Kimmel et al. reported that higher levels of perceived social support were significantly associated with decreased relative mortality risk, controlled for variations in patients' age, severity of illness, serum albumin concentration and dialyzer type [10].

In these studies, however, the effects of other potential medical risk factors, including biochemical markers and extended analysis of sociodemographic factors, were not assessed. Another study reported

that social support (interaction) was not associated with survival, neither in the whole analyzed sample nor when stratified by therapy modality [11].

Aim

The aim of the present study was to assess survival in patients on hemodialysis according to factors including gender, age, BMI, clinical and sociodemographic factors. The clinical factors analyzed in this study included time of hemodialysis, presence of comorbidities as diabetes mellitus, hypertension, cardiovascular diseases, heart failure, pulmonary diseases, stroke, kind of nephropathy, hemoglobin, AST, ALT, serum calcium, phosphate, total protein and albumin concentration. The sociodemographic factors analyzed in this study included patients' opinions on family support, living in an urban or non-urban location, level of education, marital status. These factors were chosen according to available data and information about factors influencing the survival time. Information about these factors was collected at the start of the study.

Material and methods

In this observational, prospective study, the survival of patients on chronic hemodialysis was observed during 7 years of observation time. We included a group of 110 dialysis patients from one dialysis clinic in Poland. In the recruitment process, 121 patients were considered eligible for the study, 4 were excluded, because they did not fulfill the inclusion criteria, and 7 because of lack of all clinical or sociodemographic data necessary for this study. The data about factors were collected at the start of the study in every patient that fulfilled the inclusion criteria. The patients enrolled in the study fulfilled the following inclusion criteria: age ≥ 18 years, hemodialysis treatment for more than 30 days prior to the start of the study, treatment of CKD for the last six months, lack of obstacles to collect interviews from the patient. Detailed information regarding mortality was obtained from The Official Polish Death Registry. The patient baseline data was collected from June 2005 to December 2005 and observation of survival was followed until May 2012. Variables were expressed as means and standard deviations (SD) or medians (Me) when data were skewed. The survival probability was presented in this study as a function of survival time. Survival time analysis was performed using Kaplan-Meier analysis. Death hazard ratios (HRs) were obtained using Cox proportional hazard models after controlling for the relevant covariates. HRs are presented with 95% confidence intervals. Differences in survival probability were also analyzed using the Gehan's generalized Wilcoxon test. The significance

level was set to $p=0.05$. The data were analyzed using Statistica, version 10 (StatSoft, Inc.).

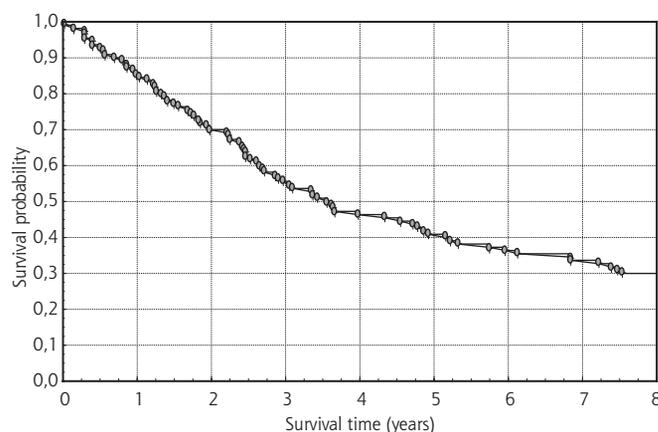
Results

The study group consisted of 110 patients, 42 women and 68 men. The average age of all patients was 59 ± 12.4 years (min 24, max 86. Me 59.5). All of the patients included in the study were observed for 7 years. The average BMI was 24.8 ± 4.46 kg/m² (Me 24.3). The average time of hemodialysis was 4.6 y (Me 2.9). In study group 24 pts had diabetes mellitus, 106 arterial hypertension, 32 cardiovascular diseases, 27 chronic heart failure, 17 had pulmonary diseases, 13 a stroke in the past, 14 patients were hemodialyzed and had previous history of kidney transplantation. The etiology of ESRD in the study was as follows: primary glomerulonephritis (25%), diabetes mellitus (21%), chronic pyelonephritis (16%), hypertension (9%), cystic kidney disease (7%), and others were below 5%. Short characteristics of biochemical factors are presented in Table I. In HD patients 64 lived in urban, 46 in non-urban areas. According to marital status 80 patients were married, 30 single. The educational level was ranked in three grades as primary school level (38 pts.), secondary school level (62 pts.) and university level (10 pts.). Satisfactory family support was reported in 19 patients in the survivors subgroup and in 28 patients in the non-survivors subgroup. The survival probability according to survival time is presented in figure 1. The 1-year survival outcome in hemodialysis patients was 85%, the 5-year one was 41%.

Patients on a Monday-Wednesday-Friday schedule had no differences in survival time according to those on a Tuesday-Thursday-Saturday schedule.

In Cox proportional hazard model, hazard ratio (HR) of death was significantly and independently related to family support (HR 0.34; CI 0.18-0.65;

$p < 0.002$); age (HR 1.05; CI 1.02-1.08; $p < 0.001$); BMI (HR 0.91; CI 0.85-0.98; $p < 0.02$); cardiovascular diseases (HR 2.07; CI 1.05-4.06; $p < 0.05$); serum calcium (HR 1.71; CI 1.34-2.18; $p < 0.001$); serum phosphates (HR 1.46; CI 1.2-1.78; $p < 0.001$) and serum albumin concentration (HR 0.35; CI 1.16-0.76; $p < 0.01$). In the non-survivors group, survival probability according to survival time between patients with and without reported satisfactory family support was presented in Figure 2. The differences in survival probability were statistically significant between these groups (Gehan’s generalized Wilcoxon test, $p < 0.05$) There was no statistical significance of living in urban and non-urban locations, marital status and level of education.



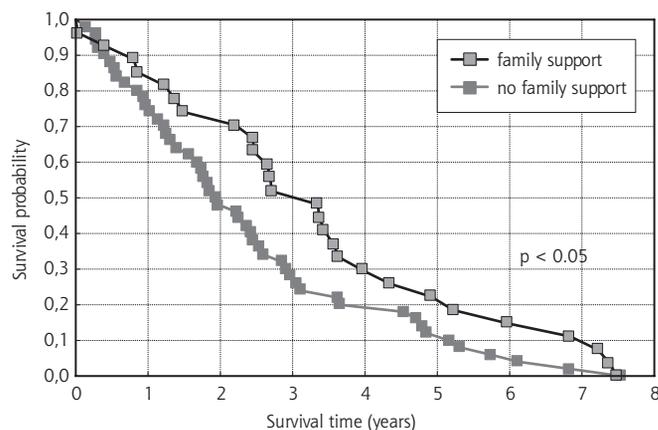
Survival probability – prawdopodobieństwo przeżycia; Survival time (years) – czas przeżycia (lata)

Fig. 1. Survival function

Ryc. 1. Funkcja przeżycia

Table I. Biochemical factors
Tabela I. Parametry biochemiczne

Biochemical factors / Parametry biochemiczne	Norm / Norma	M	SD	Me
Hb [g/dl])	female /kobiety 11.5-16.5 men /mężczyźni 12.5-18.0	10.2	1.3	10.2
AST (U/l)	5-40	21.2	14.2	17
ALT (U/l)	5-40	21.8	19	16
calcium /wapń (mg/dl)	8.5-10.5	9.4	2.3	8.9
phosphate /fosfor (mg/dl)	2.5-5.0	2.7	0.83	2.8
serum total protein /białko (g/l)	6-8	7.3	5.6	6.6
serum albumin /albuminy (g/l)	4.3-51	3.8	0.4	3.8



Survival probability – prawdopodobieństwo przeżycia; Survival time (years) – czas przeżycia (lata); family suport – obecne wsparcie ze strony rodziny; no family suport – brak wsparcia ze strony rodziny

Fig. 2. Survival function and family support

Ryc. 2. Funkcja przeżycia a wsparcie ze strony rodziny

Discussion

This study provides information on survival in ESRD patients on hemodialysis, using prospective observation from one center study in Poland. Many known or suspected factors were taken into consideration in the analysis of survival time. Age is a widely known risk factor for death in the ESRD population on dialysis. In comparison of the study the general population death rates were higher in younger patients than in older patients because mortality rates were very low in the young population and standardized mortality ratios decreased when age increased [12]. In this paper, the statistical analysis results showed that age was independently related to survival in hemodialysis patients. Early identification of individuals and the prevention of progressive CKD could be one of the key factors in reducing the CKD-associated mortality.

In this study, BMI was a factor that could independently influence survival time. It is well known that high BMI predicts mortality and cardiovascular disease (CVD) in the general population. However, observational reports in the dialysis population have suggested that obesity is associated with improved survival. BMI was also analyzed according to mortality of hemodialysis patients. In one study, the predictive value of anthropometric parameters on mortality in hemodialysis patients pointed out that mid-arm circumference was the most predictive independent marker for mortality of hemodialysis patients, but BMI was not a risk factor [13]. A large number of studies have evaluated the relationship between body size and mortality in dialysis patients. At ESRD stage, the effect of being overweight ($\text{BMI} \geq 25 \text{ kg/m}^2$) has been repeatedly associated with improved survival whereas, $\text{BMI} < 19 \text{ kg/m}^2$ was associated with increased mortality [14, 15] and weight loss in the hemodialysis population is associated with increased cardiovascular and all-cause mortality [16]. The malnutrition-inflammation-cachexia syndrome was proposed to explain the increased mortality risk of low BMI in the hemodialysis population.

It was reported that the implications of weight gain or loss may, however, differ between obese individuals and their non-obese counterparts in HD patients on hemodialysis [17]. In this study, it was also suggested that mortality in HD patients could also be associated with weight changes and a patients' BMI modifies the strength of the association between weight changes with mortality. A high BMI was associated with lower mortality in patients undergoing hemodialysis. Short-term weight gains and losses are also related to lower and higher mortality risk, respectively. The other large analyses ($n=70028$) reported that both BMI and body composition are strong predictors of death. The

protective effect conferred by high BMI was limited to those patients with normal or high muscle mass. High BMI patients with inferred high body fat have increased, not decreased mortality [18].

Cardiovascular diseases (CVD) are the major cause of death in patients on dialysis [19]. In the United States, the survival of patients on hemodialysis after 1 year was 79%, with survival after 5 years of 34%. In our group, the 1-year survival of hemodialysis patients was 85%, the 5-year survival was 41%. This analysis confirmed the important role of CVD in predicting mortality in dialyzed patients. This information is also important according to the information that early regular nephrology referral above 12 months before initiation of HD was associated with a reduced risk of all-cause and cardiovascular mortality in HD patients [20].

Accelerated atherosclerosis was reported to be an important cause of cardiovascular death in long-term dialysis patients [21] and showed strong association with mineral and bone disorders (MBD) in these patients [22]. Serum phosphorous, calcium and parathyroid hormone (PTH) levels help to assess MBD in these patients; however, a recent meta-analysis in CKD patients suggested that only serum phosphorous levels are a strong and independent predictor of mortality [23]. Mineral metabolism parameters may play a role in the survival of CKD patients. In the CORES study, abnormalities in serum levels of calcium or phosphorus were associated with increments in all-cause mortality [24]. Our study also confirmed the important role of calcium and phosphorus in predicting survival time in HD patients.

The serum albumin concentrations were reported to be as an independent predictor of survival in HD patients in our analysis. It was also pointed out that hypoalbuminemia could predict all-cause and CVD mortality in HD patients and an increase in serum albumin over time could be associated with better survival [25]. One study reported that hypoalbuminemia was associated with higher mortality also in PD patients after 7 years [26]. One study analyzed the mortality and morbidity of HD patients and showed that the patients with adverse outcomes had significantly lower serum albumin levels ($p < 0.01$) [27]. Another large ($n=78420$), cohort study on adult maintenance HD patients reported an association of serum albumin level, serum phosphorus level and hemoglobin level with both mortality and hospitalization in HD patients [28].

Four thousand and seventy-three patients from Europe, 1592 patients from Asia, 4512 patients from Latin America, and 2775 patients from the USA were studied according to the role of diabetes in mortality rate in HD patients [29]. Across all databases,

lower age and higher serum albumin levels were associated with reduced mortality. Diabetes mellitus was associated with poorer outcomes in all non-US databases; male gender was associated with poorer outcomes in all non-European databases; phosphorus levels were not associated with outcomes in any of the databases; higher post-dialysis weight was related to survival in Europe and Latin America [30]. This study does not confirm the relationship between survival time and the days of the week and dialysis schedule.

This study also reported the important role of family support in predicting survival time. Patients with family support can reach better adaptation levels, which allow them to modify their way of life, improve their quality of life (QoL) and to keep satisfactory compliance. All these factors play an important role in treatment of HD patients and may improve their survival time. It is of particular interest that HD patients, provided with a caregiver's assistance but who choose to 'act by themselves', do have better

adaptation levels and QoL than those who rely only on their family caregiver [31]. The extended analysis of this problem requires further research on health care among patients on hemodialysis. Family support should be considered in comprehensive approach to treatment.

Conclusions

1. Family support in health care on hemodialysis patients may be related to survival time independently of clinical factors.
2. The prospective, one-center study on Polish hemodialyzed patients confirmed a statistically significant relationship of survival time with age, body mass index, cardiovascular diseases and serum calcium, phosphorus and albumin level.
3. The study results may be helpful in treatment of hemodialyzed patients and building strategies focused on improvement of health care.

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