Survival Factors in Patients With End-stage Renal Disease in Mazandaran Province, Iran

Bizhan Shabankhani,[1] Anoushirvan Kazemnejad,[2] Farid Zaeri,[3] Fatemeh Espahbodi,[4] Mahmoud Haji Ahmadi,[5] Roksana Mirkazemi[6]

[1]Faculty of Biostatistics, School of Public Health, Mazandaran University of Medical Sciences, Sari, Iran
[2]Department of Biostatistics, Faculty of Medicine, Tarbiat Modares University, Tehran, Iran
[3]Department of Biostatistics, Faculty of Paramedical Sciences, Shahid Beheshti University of Medical Sciences, Tehran, Iran
[4]Faculty of Medicine, Mazandaran University of Medical Sciences, Sari, Iran
[5]Department of Biostatistics. Babol University of Medical Sciences, Babol, Iran
[6]Hooman Research Collaborators Institute, Tehran, Iran

Keywords. survival analysis, hemodialysis, Cox proportional hazard regression

Introduction. Survival analysis for patients with end-stage renal disease and factors influencing their survival is crucial due to the increase in the number of these patients along with their high mortality rate. This study aimed to analyse the survival rate of patients in north of Iran undergoing hemodialysis and to assess factors influencing their survival.

Materials and Methods. A historical cohort study was conducted on 500 patients on maintenance hemodialysis in 3 hospitals of 2 cities (Sari and Babol) in Mazandaran province during a 6-year period from 2007 to 2013. The Cox regression analysis was used to assess the impact of sex, age, education, smoking habit, primary cause of kidney failure, living with family, cardiovascular diseases, weight, age at diagnosis, and age at initiating hemodialysis on survival of the patients.

Results. The median survival time for the 500 hemodialysis patients was 108 months. Death occurred in 174 patients (34.8%). History of smoking, age, being unemployed, being illiterate, and renal cyst, congenital diseases, and unspecified diseases as the cause of kidney failure were the associated factors with survival of the patients. The 1-, 2-, 3-, 5-, 10-, and 12-year survival for these patients was estimated to be 84%, 77%, 71%, 58%, 43%, and 33%, respectively.

Conclusions. This study showed a high level of mortality and poor survival prognosis for patient undergoing maintenance hemodialysis. History of smoking, age, being unemployed, being illiterate, and renal cyst, congenital diseases, and unspecified conditions as the cause of kidney failure were the associated factors with survival of these patients.

IJKD 2016;10:79-84
www.ijkd.org

Original Paper

INTRODUCTION

End-stage renal disease (ESRD) is the near-total loss of kidney function.[1] The prevalence of ESRD has been rising globally. The prevalence of ESRD has become doubled in the United States during the last decades.[2,3] It was estimated that there would be 129 200 new patients, 651 330 long-term ESRD patients and 520 240 dialysis patients, with a cost around $ 28.3 billion by 2010 in the United States.[4] Despite recent advances, mortality in patients with ESRD remains high all around the world.[5-7] Some studies showed a 1-year mortality rate of 20% among patients undergoing haemodialysis in the United States.[8,9] However, as survival is dependent on the level of care that patients receive, survival rate varies in different countries.[10-12]

Renal replacement therapy could provide a permanent treatment for patients with ESRD; however, despite the advances in kidney

transplantation, dialysis is still one of the main mode of care and survival for the patients with ESRD; around 70% of the patients are on hemodialysis treatment.[13-15]

The Ministry of Health and Medical Education of Iran has reported the prevalence of kidney failure as 2.5 per 1000 population in Iran. It was estimated that there is an annual growth of 12% in the prevalence of this disease in 2006. Low rate of transplants make hemodialysis the main therapy for this patients in Iran.[16] Haghighi and colleagues reported that in Iran, 53.7% of ESRD patients use hemodialysis as their treatment modality; peritoneal dialysis is very uncommon (< 1%) and home hemodialysis is not performed.[17]

Survival analysis for patients with ESRD and factors influencing their survival, have become an important issue due to increase in the number of patients along with their high mortality rate (10 to 20 times compared to the general population). The purpose of this study was to analyse the survival rate of patients undergoing hemodialysis in Mazandaran, a province in north of Iran, and factors influencing their survival using Cox proportional hazard regression model, which is one of the main and the most commonly used methods for survival analysis.[18]

MATERIALS AND METHODS

Study Design and Population

A historical cohort study was conducted among ESRD patients in 3 hospitals on 6 years' data from year 2007 to the year 2013. Hospitals were located in Sari (2 hospitals) and Babol (1 hospital), two cities in Mazandaran, north of Iran. The primary study population were all patients (n = 500) who initiated maintenance hemodialysis between April 1st of 2007 to March 31st of 2013.

Data Collection

The data were collected retrospectively using medical records, including the following: sex, age, education, history of smoking, primary cause of kidney failure, family support (living with family), cardiovascular diseases, body mass index, age at diagnosis, and age at initiating hemodialysis. Detailed records of mortality information were also collected.

Death of patients due to or as a consequence of kidney failure was considered as the failure outcome in survival analysis. Patients that were lost to follow-up due to any reason and those who died due to reasons not related to kidney failure were considered as lost to follow-up. Age was considered as a remark of time duration.

Statistical Analyses

A Cox proportional hazards regression model was used to estimate mortality (hazard) ratios. Patients contributed person-time till they underwent kidney transplantation, or voluntarily withdrew from hemodialysis, died, or reached the end of the follow-up period, whichever occurred first. In the primary univariable Cox regression, proportional hazard assumption was assessed. Variables significantly associated with mortality were included in the multivariable Cox regression model. The Cox model included the following baseline variables: sex, age, education, smoking habit, primary cause of kidney failure, living with family, cardiovascular diseases, weight, age at diagnosis, and age at initiating hemodialysis. Coefficients were estimated using the maximum likelihood method and the significance of associations was tested by the Wald and likelihood tests. Data was analyzed using the SPSS software (Statistical Package for the Social Sciences, version 20.0, SPSS Inc, Chicago, IL, USA) and the Stata (version 13.0, StataCorp LP, College Station, TX, USA). A *P* value less than .05 was considered significant.

RESULTS

Characteristics of Patients

The mean age of the patients was 48.37 ± 17.87 years at diagnosis of kidney failure, 55.94 ± 17.44 years at initiating hemodialysis, and 60.13 ± 16.84 years at the end of the study period. Demographic, socioeconomic, and clinical characteristics of the patients are summarized in Table 1.

Survival Analysis

The median survival time for 500 hemodialysis patients was 108 months. During the study period, death occurred in 174 patients (34.8%). The death rate was 37.7% in males and 31.5% in females. One-, 2-, 3-, 5-, 10-, and 20-year survival rates for the patients was estimated to be 84%, 77%, 71%, 58%, 43% and 33%, respectively. Table 2 shows the cumulative hazard estimation for the hemodialysis patients in this study.

Table 1. Characteristics of Hemodialysis Patients

Characteristic	Value (%)
Sex	
Male	268 (53.6)
Female	232 (46.4)
Educational level	
Illiterate	221 (44.3)
Primary school	170 (34.1)
Diploma	79 (15.8)
Bachelor's and higher degrees	29 (5.8)
Occupation	
Housewife	206 (41.2)
Unemployed	104 (20.8)
Employee	31 (6.2)
Farmer	35 (7.0)
Retired	67 (13.4)
Others	57 (11.4)
History of smoking	77 (16.2)
CVD history	224 (46.6)
Primary cause of kidney failure	
Diabetes mellitus	231 (46.2)
Hypertension	99 (20.0)
Nephrolithiasis	25 (5.0)
Renal cysts	11 (2.2)
Congenital	24 (4.8)
Unknown	82 (16.5)
Others	24 (4.8)
Marital status	
Single	38 (7.6)
Married	410 (82.5)
Widowed	45 (9.1)
Divorced	4 (0.8)
Living with family	414 (87.7)

Factors Associated With Survival

The log marginal likelihood regression of univariable Cox model showed that there was a significant association between survival of patients and age, primary cause of kidney failure, occupation, and smoking history. There was no significant association between survival of patients and other variables. Table 3 shows the mean and median survival of patients in reference to their smoking history, primary cause of kidney failure, and occupation. The median survival for those who reported a history of smoking was 60 months, while it was 132 months for nonsmokers. Minimum median survival was for those with congenital and unknown primary cause of kidney failure (48 months) and maximum for those with nephrolithiasis as the primary cause of kidney failure (546 months). Farmers had minimum median survival (24 months).

Table 3. Median Survival of Patients by Smoking History, Primary Cause of Kidney Failure, and Occupation

Variable	Median (%95 Confidence Interval)
History of smoking	
Yes	60 (38.6 to 81.4)
No	132 (59.6 to 204.4)
Cause of dialysis	
Diabetes	96 (66.1 to 125.9)
Hypertension	…
Nephrolithiasis	564
Renal cyst	252 (0.0 to 571.5)
Congenital	48 (31.0 to 65.0)
Others	48 (5.2 to 90.8)
Occupation	
Housewife	96 (62.5 to 129.5)
Unemployed	444 (3.9 to 884.1)
Employee	84 (10.1 to 157.9)
Farmer	24 (0.0 to 49.0)
Retired	60 (32.6 to 87.4)
Others	72 (42.4 to 101.6)

Table 4 shows the final result of survival model fitness of multivariable Cox analysis. Age of the patient was significantly associated with survival rate ($P < .001$). Sex, body weight, history of cardiovascular disease, and age at initiating hemodialysis did not have any significant association with survival rate. Death hazard was 36% less in those who had a primary level of education compared to illiterates. Unemployment was significantly associated with survival. Those who were unemployed had a significantly lower death hazard ($P = .03$). Those who had no history of smoking had 39% less death hazard compared

Table 2. Cumulative Hazard Estimation of Mortality for Hemodialysis Patients

Survival Time, mo	Number of Patients	Death	Lost to Follow-up	Cumulative Hazard (95% Confidence Interval)
12	436	39	59	0.1615 (0.1986 to 0.1307)
24	338	25	51	0.2285 (0.2716 to 0.1914)
36	262	18	50	0.2871 (0.3352 to 0.2447)
60	146	16	35	0.4184 (0.4785 to 0.3632)
120	45	3	9	0.5732 (0.6490 to 0.4996)

Table 4. Multivariable Cox Regression Analysis of Variables Associated With Mortality Hemodialysis Patients

Variable	Coefficient	Standard Error	Hazard Ratio	*P*
Age	0.032	0.005	1.033	< .001
Weight	0.004	0.007	1.004	.54
Age at initiating hemodialysis	0.001	0.006	1.000	.97
Female sex	- 0.801	0.407	0.449	.09
Education (illiterate as referent)				
Primary school	- 0.444	0.255	0.641	.03
Diploma	-0.042	0.272	0.958	.88
Bachelor's or higher	0.479	0.401	1.615	.23
Married status (single as referent)	0.362	0.240	1.436	.13
Occupation (housewife as referent)				
Employee	-0.767	0.568	0.464	.18
Farmer	-0.489	0.542	0.614	.37
Retired	-0.590	0.531	0.544	.27
Others	-0.702	0.549	0.495	.20
Unemployed	-0.996	0.469	0.369	.03
Primary cause of kidney failure (diabetes as referent)				
Hypertension	-0.717	0.390	0.488	.07
Nephrolithiasis	-1.180	0.723	0.307	.10
Renal cyst	-1.713	0.751	0.180	.02
Congenital diseases	0.798	0.205	2.221	.001
Others	0.663	0.312	1.942	.03
No history of smoking	-0.492	0.208	0.611	.02
No history of cardiovascular disease	0.111	0.164	1.117	.50

to those with a smoking history (P = .02). Death hazard was higher among patients with congenital diseases and other or unspecified cause of kidney failure compared to those with diabetes mellitus (Table 4).

DISCUSSION

This study analyzed survival among 500 patients with ESRD and factors associated with their survival in 3 hospitals located in 2 cities in north of Iran during 6 years. This study showed a median survival time of 108 months and a mortality rate of 34.8% during 6 years' study.

In a 2-year prospective study, Chandrashekar and colleagues reported a mortality rate of 19.8% among 96 patients with ESRD at a tertiary care hospital in India, which is higher than the 2-year mortality rate (5.0%) in this study. Another study from Italy comparing dialysis patients with the general population showed that a 5-year relative survival estimate was 55.6%.[20] However, while showing high level of mortality among patient with ESRD, this figure is not comparable with our study, as the researchers used the excess mortality rate, but not the simple proportion of survivors. Montazeri and coworkers studied 5-year survival rates among 200 hemodialysis patients attending a hospital in north of Iran, using Kaplan-Meier method[21]; they showed a survival rate of 75% for 1 year and 23% for 5 years, which are below the survival rate in this study. Variation in methodological approaches or differences in the level of care in different hospitals may have contributed to these different findings in these studies.[21] Mazzuchi and coworkers compared survival for hemodialysis patients versus kidney transplant recipients treated in Uruguay and showed 1-, 5-, and 10-year survival rates of 90.6%, 62.7%, and 39.8%, which are similar to the findings in this study.[22]

This study showed that diabetes mellitus and hypertension are the main primary causes of kidney failure in the patients. Similar reports have been published by many other studies in Iran.[17,23,24] Also, this study showed that farmers had the poorest survival duration, which may be due to disparity in access to care centers for farmers in rural and remote areas. Unemployed patients had the highest median survival rate, which may be a reflection of more available time for treatment or less physical distress.

Survival model fitness of multivariable Cox analysis in this study showed that a history of

smoking, age, being unemployed, being illiterate, and having renal cyst, congenital disease, and unspecified causes of kidney failure were the associated with survival or mortality of the patients. Similarly, in the study of Nordio and coworkers, it was shown that older age, systemic diseases, and diabetes mellitus had the strongest associations with mortality.[20] Liem and colleagues compared hemodialysis and peritoneal dialysis survival rates in the Netherlands and found that diabetes mellitus was associated with reduced survival in both groups.[25] Sa Carvalho and associates showed that age and diabetes mellitus as underlying cause of disease were the main risk factors for survival,[26] but Chandrashekar and colleagues' study in India found no significant difference in mortality between diabetic and nondiabetic patients.[19] Smoking prevention and increase in literacy level (which have an impact on the level of awareness of individuals) were the only modifiable risk factors that found to be effective in the increase in survival rates of hemodialysis patients in this study. The main limitation of this study was that the impact of some important variables such as the frequency of hemodialysis and comorbidities on survival were not assessed.

CONCLUSIONS

This study showed a high level of mortality and poor survival prognosis for patient with ESRD undergoing maintenance hemodialysis. Diabetes mellitus and hypertension were the main primary causes of kidney failure in the patients. History of smoking, age, being unemployed, being illiterate, and renal cyst, congenital diseases, and unspecified conditions as the cause of kidney failure were the associated factors with survival of patients.

CONFLICT OF INTEREST

None declared.

REFERENCES

1. Kao WH, Klag MJ, Meoni LA, et al. MYH9 is associated with nondiabetic end-stage renal disease in African Americans. Nat Genet. 2008;40:1185-92.
2. [No author listed]. USRDS: the United States Renal Data System. Am J Kidney Dis. 2003;42:1-230.
3. Hsu CY, McCulloch CE, Iribarren C, Darbinian J, Go AS. Body mass index and risk for end-stage renal disease. Ann Intern Med. 2006;144:21-8.
4. Xue JL, Ma JZ, Louis TA, Collins AJ. Forecast of the number of patients with end-stage renal disease in the United States to the year 2010. J Am Soc Nephrol. 2001;12:2753-8.
5. Duman D, Tokay S, Toprak A, et al. Elevated cardiac troponin T is associated with increased left ventricular mass index and predicts mortality in continuous ambulatory peritoneal dialysis patients. Nephrol Dial Transplant. 2005;20:962-7.
6. Tonelli M, Wiebe N, Culleton B, et al. Chronic kidney disease and mortality risk: a systematic review. J Am Soc Nephrol. 2006;17:2034-47.
7. Murtagh FE, Addington-Hall J, Higginson IJ. The prevalence of symptoms in end-stage renal disease: a systematic review. Adv Chronic Kidney Dis. 2007;14:82-99.
8. Ariyamuthu VK, Nolph KD, Ringdahl BE. Periodontal disease in chronic kidney disease and end-stage renal disease patients: a review. Cardiorenal Med. 2013;3:71-8.
9. Foley RN, Parfrey PS, Sarnak MJ. Clinical epidemiology of cardiovascular disease in chronic renal disease. Am J Kidney Dis. 1998;32:S112-S119.
10. Wen CP, Cheng TY, Tsai MK, et al. All-cause mortality attributable to chronic kidney disease: a prospective cohort study based on 462 293 adults in Taiwan. Lancet. 2008;371:2173-82.
11. deFilippi C, Wasserman S, Rosanio S, et al. Cardiac troponin T and C-reactive protein for predicting prognosis, coronary atherosclerosis, and cardiomyopathy in patients undergoing long-term hemodialysis. JAMA. 2003;290: 353-9.
12. Yang WC, Hwang SJ. Incidence, prevalence and mortality trends of dialysis end-stage renal disease in Taiwan from 1990 to 2001: the impact of national health insurance. Nephrol Dial Transplant. 2008;23:3977-82.
13. Jones CA, McQuillan GM, Kusek JW, et al. Serum creatinine levels in the US population: third National Health and Nutrition Examination Survey. Am J Kidney Dis. 1998;32:992-9.
14. Parmar MS. Chronic renal disease. BMJ. 2002;325:85-90.
15. Brunner FP, Brynger H, Challah S, et al. Renal replacement therapy in patients with diabetic nephropathy, 1980-1985. Report from the European Dialysis and Transplant Association Registry. Nephrol Dial Transplant. 1988;3:585-95.
16. Ghods AJ, Ossareh S, Savaj S. Results of renal transplantation of the Hashemi Nejad Kidney Hospital--Tehran. Clin Transpl. 2000;203-10.
17. Haghighi AN, Broumand B, D'Amico M, Locatelli F, Ritz E. The epidemiology of end-stage renal disease in Iran in an international perspective. Nephrol Dial Transplant. 2002;17:28-32.
18. Fan J, Li R. Variable selection for Cox's proportional hazards model and frailty model. Ann Stat. 2002;30:74-99.
19. Chandrashekar A, Ramakrishnan S, Rangarajan D. Survival analysis of patients on maintenance hemodialysis. Indian J Nephrol. 2014;24:206-13.
20. Nordio M, Limido A, Maggiore U, Nichelatti M, Postorino M, Quintaliani G. Survival in patients treated by long-term dialysis compared with the general population. Am J Kidney Dis. 2012;59:819-28.

21. Montaseri M, Charati JY, Espahbodi F, Mousavi SJ. Five-year survival rate in hemodialysis patients attending Sari Imam Khomeini Hospital. J Mazandaran Univ Med Sci. 2013;23:78-85.
22. Mazzuchi N, Gonzalez-Martinez F, Carbonell E, Curi L, Fernandez-Cean J, Orihuela S. Comparison of survival for haemodialysis patients vs renal transplant recipients treated in Uruguay. Nephrol Dial Transplant. 1999;14:2849-54.
23. Aghighi M, Heidary RA, Zamyadi M, et al. Dialysis in Iran. Iran J Kidney Dis. 2008;2:11-5.
24. Aghighi M, Mahdavi-Mazdeh M, Zamyadi M, Heidary RA, Rajolani H, Nourozi S. Changing epidemiology of end-stage renal disease in last 10 years in Iran. Iran J Kidney Dis. 2009;3:192-6.
25. Liem YS, Wong JB, Hunink MG, de Charro FT, Winkelmayer WC. Comparison of hemodialysis and peritoneal dialysis survival in The Netherlands. Kidney Int. 2007;71:153-8.
26. Sa Carvalho M, Henderson R, Shimakura S, Sousa IP. Survival of hemodialysis patients: modeling differences in risk of dialysis centers. Int J Qual Health Care. 2003;15:189-96.

Correspondence to:
Anoushirvan Kazemnejad
Department of Biostatistics, Faculty of Medicine, Tarbiat Modares University, PO Box 14115-111, Tehran, Iran
Tel: +98 911 154 3915
E-mail: kazem_an@modares.ac.ir

Received July 2015
Revised November 2015
Accepted November 2015