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Survival by Time of Day of Hemodialysis in Korean Patients: A Single Center Study

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Authors' contributions

This work was carried out in collaboration between all authors. Authors BRK and HSS participated in the design of the study and performed the statistical analysis. Authors JHP, YSJ and HR conceived of the study and participated in its design and coordination. All authors read and approved the final manuscript.

Research Article

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ABSTRACT

Background: Patients with end-stage renal disease (ESRD) typically undergo hemodialysis (HD) during the morning or afternoon, with time of treatment generally based on space availability or patient preference. No studies have investigated variation in patient survival as a function of the time of day of dialysis in Korean HD patients. We investigated the association of patient HD treatment shift with continued survival, controlling for well-established HD-related mortality risk factors.
Method: A 10-year (from January 1, 2001 to December 31, 2010) follow-up retrospective cohort study was conducted among 120 ESRD patients who underwent HD at Kosin University Gospel Hospital either during a morning shift (n = 60) or an afternoon shift (n = 60). A variable comparison was conducted using a Chi-square test and t-test for categorical and continuous variables, respectively. Life table analysis was used to compare survival rates in the two treatment groups.
Results: The mean survival rate of the morning-shift HD patients and afternoon-shift HD patients were not statistically different (mean survival, 61.1 months vs. 48.2 months; P = 0.139). The unadjusted 5-year survival rate for patients on morning shift hemodialysis was 87.3% versus 86.4% for patients on afternoon shift hemodialysis (P = 0.704 by Wilcoxon test).
Conclusions: The survival rates of morning-shift HD patients and afternoon-shift HD

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patients were not different. Results from this cohort study may warrant prospective observational studies and randomized clinical trials in Korean HD patients for whom the time of day at which HD is administered is systemically varied.

Keywords: End-stage renal disease; morning shift hemodialysis; afternoon shift hemodialysis; time of day.

1. INTRODUCTION

Every year in Korea, more than 50,000 patients receive treatment for ESRD, and most of these patients receive in-center HD throughout the course of their illness. The proportion of patients receiving HD among end-stage renal disease patients (ESRD), including all patients on HD, peritoneal dialysis and after renal transplantation, has increased to 70% in Korea [1]. Approximately 70% of these patients have a 5-year survival rate, and cause of death is associated with multiple risk factors. Patients typically undergo hemodialysis (HD) during the morning or afternoon, with time of treatment generally based on space availability or patient preference. To our knowledge, no studies have investigated the variation in Korean HD patient survival as a function of the time of day that they receive dialysis. We investigated the association of patient HD treatment shift with their continued survival, controlling for well-established HD-related mortality risk factors.

2. MATERIALS AND METHODS

2.1 Study Population

2.1.1 Subjects

Cohorts comparison was performed and 120 stable patients on maintenance HD at Kosin University Gospel Hospital in Busan, Korea enrolled over a 10 year period and were followed for a maximum 120 months, from January 2001 to December 2010. Over this period, 200 patients were screened for enrollment and 80 excluded form analysis: Twenty patients were lost to follow up, 20 withdrew consent, 5 started peritoneal dialysis and 35 patients sought treatment at another clinic. Inclusion criteria were HD therapy for more than three months and a stable condition with no severe co-morbidities, such as cardiovascular disease, respiratory disease, gastrointestinal disease, neurologic disease, acute illness, malignancy, or severe infection. All patients were receiving maintenance HD three times a week for 4.1 ± 0.5 hours per session, with hollow-fiber dialyzers and a bicarbonate buffered dialysate containing 100 mg/dL glucose and 30 mq/L bicarbonate. The blood flow rate was greater than 200 mL/min, and the dialysate flow rate was 500 mL/min. The study protocol was approved by the ethics committee of Kosin University Gospel Hospital.

2.2 Determination of Dialysis Shift and Medical History

Patients whose in-center HD was initiated between 8:00 AM and 12:00 PM were considered as having morning dialysis (n = 60). Patients whose in-center dialysis was initiated between 12:00 PM and 4:00 PM were considered to have undergone afternoon dialysis (n = 60). Demographic or health-status characteristics were not different between cases regarding shift dialysis. There was no significant difference in the number of months of dialysis before the study or in post-study survival between included and excluded patients. We assessed the time of the dialysis shift in the study period per 6 months. The nursing experience and staff-patient ratios for the morning and afternoon shifts were identical. The same nephrologist took care of patients before and after morning and afternoon shifts.

A comprehensive interview and a review of medical records were conducted for all patients at the beginning of the study and for patients participating in the 10-year follow-up. Characteristics of HD (months of dialysis before study entry and number of hours of dialysis per week) were confirmed by the dialysis facility, as was history of diabetes mellitus as a primary cause of ESRD. Body mass index (BMI; computed as weight in kilograms divided by squared height in meters) and serum albumin level were also recorded. We collected clinical data such as sex, age, body mass index, presence of type 2 diabetes mellitus and laboratory results from patient charts. Blood laboratory tests were performed once a month and the results from three individual months were averaged. Body weight (dry weight) was measured after each dialysis session, and BMI was calculated using dry weight.

2.3 Statistical Analysis

Data are expressed as mean ± SD. Comparisons were performed using Chi-square and t-test for categorical and continuous variables, respectively. Life table analysis was used to compare survival in both treatment groups. *P*-values for comparison of survival curves were determined using the Wilcoxon test. The relative risks of mortality for different parameters were estimated using Cox proportional hazards models. Hazard ratios and 95% confidence intervals (CI) were calculated using the estimated regression coefficients and standard errors in Cox regression analysis. *P*-values < 0.05 were considered statistically significant. All statistical analyses were performed using Statistical Package for the Social Sciences (SPSS), version 18.0 (SPSS Inc., Chicago, IL, USA).

3. RESULTS

3.1 Baseline Clinical Characteristics

One hundred twenty patients were included in this study (morning-shift HD patients; N = 60, 50%, afternoon-shift HD patients; N = 60, 50%). Table 1 lists patient demographic and treatment characteristics by time of day of hemodialysis. Afternoon-shift hemodialysis patients were older than morning-shift cases (p=0.008). The mean survival rate of the morning-shift HD patients and afternoon-shift HD patients were not statistically different (mean survival, 61.1 months vs. 48.2 months; P = 0.139). The prevalence of diabetes was 48% in all subjects. Normalized protein catabolic rate (nPCR), blood urea nitrogen, phosphorus, uric acid and CRP were statistically different between the two groups but the rest of the parameters were not.

3.2 Survival Rates of Morning-shift and Afternoon-shift HD Patients

The results of univariate tests of association with the Cox regression model for continued patient survival in days after the beginning of the study are summarized in Table 2. Age, gender, diabetes, BMI and morning dialysis shift were not significantly associated with continued HD patient survival (all P > 0.05). Table 3 presents the results of the multivariable Cox model predicting survival according to demographic and health variables, as well as time of day of dialysis. A Cox proportional hazards model indicated that the morning shift did not result in a protective effect (relative risk, 0.793; 95% confidence interval, 0.198-3.181) independent of age, sex, body mass index, diabetic ESRD, and months of dialysis in this multivariable model. The unadjusted five-year survival rate for patients on morning shift HD was 87.3% versus 86.4% for patients on afternoon shift HD (P = 0.704 by the Wilcoxon test) (Fig. 1).

Table 1. Characteristics by hemodialysis shift

Variable	Morning shift	Afternoon shift	P
Age (years)	53.1 ± 10.5	59.2 ± 14.0	0.008
Male/Female	29/31	22/38	0.196
Diabetes (−/+)	36/24	26/34	0.068
Survival (−/+)	6/54	5/55	0.752
HBs Antigen (−/+)	55/5	58/2	0.243
HCV Antibody (−/+)	58/2	55/5	0.243
VDRL (−/+)	58/2	57/3	0.648
Mean survival rate (months)	61.1 ± 42.3	48.2 ± 55.5	0.139
Kt/V	1.38 ± 0.37	1.36 ± 0.30	0.718
Urea reduction rate (%)	66.7 ± 9.5	66.6 ± 8.6	0.955
Body mass index	22.0 ± 2.7	22.4 ± 4.5	0.631
Systolic blood pressure (mmHg)	141 ± 30	143 ± 22	0.618
Diastolic blood pressure (mmHg)	84 ± 13	79 ± 11	0.057
Ultrafiltration (kg)	2.7 ± 1.5	2.6 ± 1.1	0.910
Hemodialysis time (minutes)	239.0 ± 7.7	238.0 ± 10.8	0.563
Total body water (L)	32.0 ± 5.1	31.0 ± 6.5	0.358
Protein catabolic rate (g/kg/day)	1.02 ± 0.35	0.82 ± 0.23	0.001
Normalized PCR (g/kg/day)	1.07 ± 0.37	0.87 ± 0.25	0.003
Hemoglobin (g/dL)	10.0 ± 0.9	10.3 ± 1.1	0.197
Iron (ug/dL)	72.3 ± 34.1	61.9 ± 31.4	0.154
TIBC (ug/dL)	269.2 ± 54.4	248.1 ± 60.6	0.108
Ferritin (ng/mL)	274.2 ± 471.9	543.5 ± 1430.2	0.241
Blood urea nitrogen (mg/dL)	72 ± 28	60 ± 19	0.009
Creatinine (mg/dL)	9.3 ± 3.6	7.1 ± 3.0	0.001
Sodium (mEq/L)	138 ± 4	138 ± 3	0.378
Potassium (mEq/L)	5.1 ± 0.8	5.0 ± 1.0	0.438
Calcium (mg/dL)	8.9 ± 0.7	8.8 ± 0.7	0.462
Phosphorus (mg/dL)	5.6 ± 1.8	5.0 ± 1.3	0.028
Parathyroid hormone (pg/mL)	204.9 ± 138.9	170.5 ± 154.7	0.293
Albumin (g/dL)	3.7 ± 0.4	3.7 ± 0.3	0.793
Total cholesterol (mg/dL)	164 ± 36	165 ± 45	0.946
HDL (mg/dL)	40 ± 11	40 ± 16	1.000
Low density lipid (mg/dL)	87 ± 30	86 ± 31	0.934
L.D.H (IU/L)	389 ± 103	495 ± 230	0.006
Uric acid (mg/dL)	8.3 ± 1.7	7.5 ± 1.4	0.018
CRP (mg/dL)	0.30 ± 0.48	1.05 ± 2.22	0.030

VDRL: Veneral Disease Research Laboratory test; PCR: Protein catabolic rate; TIBC: Total Iron Binding Capacity; HDL: High density lipoprotein; LDH: Lactate dehydrogenase; CRP: C-reactive protein

Table 2. Univariate cox proportional hazards analysis of mortality

Variable	Unit increase	Hazard ratio (95% CI)	P
Morning dialysis shift	vs. afternoon shift	1.242 (0.378−4.083)	0.721
Age	Years	1.042 (0.988−1.098)	0.127
Gender	vs. male	1.518 (0.458−5.024)	0.495
Diabetes	vs. absence	2.958 (0.857−10.205)	0.086
BMI	1	0.830 (0.671−1.025)	0.084

Table 3. Multivariate cox proportional hazards analysis of mortality

Variable	Unit increase	Hazard ratio (95% CI)	P
Morning dialysis shift	vs. afternoon shift	0.793 (0.198−3.181)	0.744
Age	Years	1.050 (0.991−1.113)	0.100
Gender	vs. male	3.002 (0.718−12.549)	0.132
Diabetes	vs. absence	2.715 (0.715−9.766)	0.126
BMI	1	0.780 (0.603−1.009)	0.058

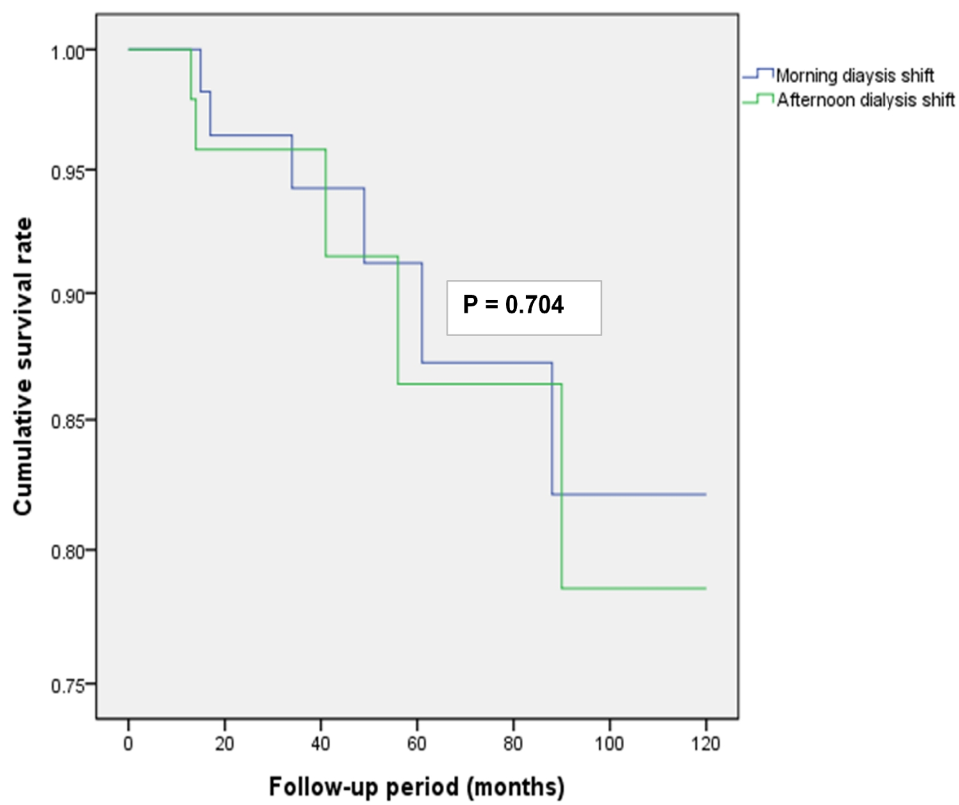

Fig. 1. Life Table Survival Curves for Patients Undergoing Dialysis during Morning and Afternoon Shifts

4. DISCUSSION

In this study, we examined the association of patient HD treatment shift with continued survival, controlling for well-established HD-related mortality risk factors. The present study showed that morning shift HD was not associated with reduced mortality compared with afternoon shift HD in a retrospective study of Korean HD patients. Patients typically undergo HD during the morning or afternoon, with time of treatment generally based on space availability or patient preference. Currently, there is little data suggesting that the time of day when HD is performed has any functional consequence for patients undergoing the procedure. However, Bliwise et al. [2] found that morning shift HD was associated with a significant reduction in mortality compared to that of patients receiving afternoon shift HD, with a relative risk of 0.71 in a cohort of elderly (60 years or older) chronic HD patients. Additionally, Kevin C. et al. reported that morning shift HD was associated with reduced mortality among patients 60 years or older compared with that of afternoon shift HD patients, but there was no significant association with mortality among younger HD patients [3].

If the time of day of dialysis significantly affects survival, some speculation regarding putative mechanisms that underlie the effect may not be premature. First, Bliwise et al. [2] speculated that morning shift HD patients might be more likely to sleep during their sessions than afternoon shift HD patients, and this might be related to the difference in survival seen between the two shifts. Individuals undergoing HD in the morning are sleepier than those being dialyzed at other times of day [4], and the notion that sleep is vital for health and that loss of sleep hastens morbidity and mortality has been supported by numerous epidemiologic human studies and experimental animal studies. For example, studies from well-defined populations suggest that chronic sleep deprivation may be a harbinger for all causes of mortality [5,6]. In experimentally sleep-deprived animals, sleep loss has been associated with compromised thermoregulatory, immunologic, and, perhaps most relevant for the current discussion, protein metabolic functions [7,8]. Such data imply that sleep during morning dialysis may impart a beneficial compensatory response to sleep loss imposed by early waking times. This explanation assumes differences in the quantity or quality of intradialytic sleep as a function of the time of day. This hypothesis remains to be polysomnographically verified. Unfortunately, sleep patterns and practices were not measured in either their study or ours. Second, it is possible that blood pressure or volume control might be more important in the early morning or evening hours than in afternoon hours because rates of both myocardial infarction and subarachnoid hemorrhage are greater in the morning [9-11]. This relationship might be more important for patients with preexisting (established) disease, who would more likely be elderly. However, there was no significant difference in pre-systolic blood pressure levels between shifts in this study. Third, biochemical clearance may be optimized during morning-shift HD. In a group of 124 patients representing four shifts, Mattana et al. [12] reported that HD patients who were dialyzed late in the day had relatively higher levels of potassium and phosphorus than those undergoing HD earlier in the day, implying less effective dialysis, perhaps owing to interaction with the evening meal. Thus, the possibility exists that some impairment of biochemical clearance might have hastened mortality in patients being dialyzed in the afternoon shift. However, our study showed that levels of potassium, phosphorus, PCR, nPCR and BUN were higher in the morning shift patients. We postulated that the nutritional state of patients receiving morning-shift HD was better than that of patients undergoing afternoon-shift HD, and that impairment of the nutritional state might have hastened mortality in patients being dialyzed in the afternoon. Fourth, the findings that time of day of dialysis significantly affects survival could be a result of confounding unmeasured variables or incomplete adjustment, given the large numbers of significant differences in variables between HD shifts (Table 1). The age difference for the afternoon shift patients was particularly remarkable, as was the percentage of patients on this shift who did not have survival times available for analysis; therefore, we urge caution in interpretation of these results.

The findings by Bliwise et al. indicating apparently protective effects of morning dialysis were observed in an elderly cohort. Whether younger patients undergoing HD would derive a similar benefit remains unclear. In the present study, morning shift HD was not associated with reduced mortality compared with that of afternoon shift HD in either of the age groups. The fifth possible cause of unmeasured bias could be the practice of reserving afternoon HD shifts for patients who were sicker or required more staffing [13]. This practice could not be documented with certainty using the USRDS database, as was the case in the study by Bliwise et al. The possible relationship between patient survival and HD unit staffing has been infrequently studied [14,15]. A recent study has shown that nurse staffing is an independent predictor of survival in hospitalized patients in the general population [16]. However, in the present study, there were no differences in months on HD before study entry according to patient shift, nor were there differences in co-morbid diseases, such as cardiovascular disease or diabetes. Survival might not be different if patients truly get to choose their shift, as patients are likely to choose the time slot that works best for their own schedules and rhythms.

We could not evaluate the employment status of the patients, which may influence both shift selection and survival because of inadequacy of medical record. These points should be studied in future prospective trials of survival by time of day of HD.

This study has several limitations. First, it is observational and not randomized; therefore, findings could still be confounded despite adjustment. Because this study was a single center study and a lack of statistical power, conclusion has a limited generalizability. Results from this cohort study may warrant prospective observational studies and randomized clinical trials that systematically alter the time of day at which HD is administered to Korean HD patients. Second, we were unable to follow-up on changes in variables over time, including changes in time or frequency of hemodialysis, blood pressure, laboratory values, or HD adequacy. This applies especially to possible changes in HD shifts, medication use, and changes in patient dry weight.

In summary, this study of a retrospective cohort of Korean HD patients showed that time of day of HD (morning and afternoon shift) was not significantly associated with survival in HD patients. As the study did not find any merit of HD shift in Korean patients, there is difficult to make the case for further studies.

CONSENT

A waiver of consent was granted from our review board because of retrospective study.

ETHICAL APPROVAL

All authors hereby declare that all human studies have been examined and approved by the appropriate ethics committee and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. ESRD Registry Committee KSoN. Current renal replacement therapy in korea- insan memorial dialysis registry, 2009. The Korean J Nephrol. 2010;29:525-551.
2. Bliwise DL, Kutner NG, Zhang R, Parker KP. Survival by time of day of hemodialysis in an elderly cohort. JAMA. 2001;286:2690-2694.
3. Abbott KC, Reynolds JC, Trespalacios FC, Cruess D, Agodoa LY. Survival by time of day of hemodialysis: Analysis of united states renal data system dialysis morbidity and mortality waves iii/iv. Am J Kidney Dis. 2003;41:796-806.
4. Parker KP, Bliwise DL, Rye DB, De A. Intradialytic subjective sleepiness and oral body temperature. Sleep. 2000;23:887-891.
5. Kripke DF, Simons RN, Garfinkel L, Hammond EC. Short and long sleep and sleeping pills. Is increased mortality associated? Arch Gen Psychiatry. 1979;36:103-116.
6. Wingard DL, Berkman LF, Brand RJ. A multivariate analysis of health-related practices: A nine-year mortality follow-up of the alameda county study. Am J Epidemiol. 1982;116:765-775.
7. Everson CA, Bergmann BM. Rechtschaffen A. Sleep deprivation in the rat: Iii. Total sleep deprivation. Sleep. 1989;12:13-21.
8. Kushida CA, Bergmann BM, Rechtschaffen A. Sleep deprivation in the rat: Iv. Paradoxical sleep deprivation. Sleep. 1989;12:22-30.
9. Fantidis P, Perez De Prada T, Fernandez-Ortiz A, Carcia-Touchard A, Alfonso F, Sabate M, Hernandez R, Escaned J, Bauelos C, Macaya C. Morning cortisol production in coronary heart disease patients. Eur J Clin Invest. 2002;32:304-308.
10. Feigin VL, Anderson CS, Rodgers A, Bennett DA. Subarachnoid haemorrhage occurrence exhibits a temporal pattern - evidence from meta-analysis. Eur J Neurol. 2002;9:511-516.
11. Peters RW, Zoble RG, Brooks MM. Onset of acute myocardial infarction during sleep. Clin Cardiol. 2002;25:237-241.
12. Mattana J, Patel A, Wagner JD, Maesaka JK, Singhal PC. Effect of time of day of dialysis shift on serum biochemical parameters in patients on chronic hemodialysis. Am J Nephrol. 1995;15:208-216.
13. Kessler DM, Kessler DH, Knibloe ME: A dialysis patient classification system for establishing nurse/patient ratios. ANNA J. 1990;17:367-370; discussion 371.
14. Held PJ, Garcia JR, Pauly MV, Cahn MA. Price of dialysis, unit staffing, and length of dialysis treatments. Am J Kidney Dis. 1990;15:441-450.
15. Held PJ, Pauly MV, Diamond L. Survival analysis of patients undergoing dialysis. JAMA. 1987;257:645-650.
16. Aiken LH, Clarke SP, Sloane DM, Sochalski J, Silber JH. Hospital nurse staffing and patient mortality, nurse burnout, and job dissatisfaction. JAMA. 2002;288:1987-1993.

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