

A Retrospective Analysis of Five Year Data of End-Stage Renal Disease Patients: A Single Center Experience

Son Dönem Böbrek Yetmezliği Hastalarının 5 Yıllık Retrospektif Analizi: Tek Merkez Deneyimi

ABSTRACT

OBJECTIVES: CKD is a worldwide threat to public health. Approximately 1.8 million people are currently being treated with renal replacement therapy including hemodialysis, peritoneal dialysis and transplantation. The etiology and factors affecting the progression of chronic kidney disease to end-stage renal disease (ESRD) differ in industrialized and underdeveloped countries.

STUDY DESIGN: The aim of the study was to investigate the etiologies of ESRD, factors affecting progression to ESRD and mortality rates of patients between 2000-2004, in Konya, a city in the Middle Anatolian region of Turkey.

MATERIAL and METHODS: We included 417 end-stage renal disease patients (207 female and 210 male) between 16-90 years old receiving RRT for the first time in the study. CKD was diagnosed by GFR measurement that was calculated by MDRD formula. Co-morbidity was expressed using Wright-Khan index.

RESULTS: We showed that there was an increased rate of diabetic nephropathy between 2003 and 2004. The increased rate of diabetic nephropathy was found to be statistically significant in the last two years ($p<0.005$). There was also significant negative correlation between mortality and diastolic BP ($r: -0.143, p: 0.05$) and the education level of the patients ($r: -0.159, p: 0.0002$). There was a positive correlation between mortality and serum urea levels ($r: 0.193, p: 0.0001$), HD through a catheter for the first time ($r: 0.140, p: 0.0006$), and receiving HD by a continuous RRT modality ($r: 0.163, p: 0.0001$).

CONCLUSION: Our study showed that advanced age, increased mean arterial BP before the first RRT, having CVD or DM as an etiology of ESRD, increased erythrocyte sedimentation rate (ESR), decreased serum albumin levels and the presence of co-morbid diseases were the main factors that affected survival of the patients.

KEY WORDS: End-Stage renal disease, Renal replacement therapy, Diabetes

ÖZ

AMAÇ: Kronik böbrek hastalığı tüm dünyayı tehdit eden bir sorundur. Yaklaşık olarak 1.8 milyon kişi periton diyalizi, hemodiyaliz ve transplantasyon ile tedavi edilmektedir. KBY etiyojisi ve ilerlemeye neden olan etmenler gelişmiş ve gelişmekte olan ülkelerde farklılık göstermektedir. Bu çalışmada 2000-2004 yılları arasında Türkiye'nin İç Anadolu bölgesinde yer alan Konya ilinde son dönem böbrek yetmezliği hastalarının etiyojileri, hastalığın ilerlemesine neden olan etmenleri ve mortalite nedenlerini araştırmayı hedefledik.

GEREÇ ve YÖNTEMLER: Çalışmamıza yaşları 16-90 arasında son dönem böbrek yetmezliği bulunan 417 hasta (207 kadın, 210 erkek) alındı. KBH tanısı MDRD formülü kullanılarak konuldu. Yandaş hastalıklar Wright-Khan ko-morbidite indeksi kullanılarak değerlendirildi.

BULGULAR: Çalışmamızda, 2003-2004 yılları arasında diyabetik nefropati sıklığında artış saptandı ($p<0.005$). Mortalite ile hastaların diyastolik kan basıncı ve eğitim durumu arasında istatistiksel olarak anlamlı negatif korelasyon saptanırken, serum üre düzeyi, HD'e kateter yoluyla girmek ve RRT olarak HD'e devam edilmesi arasında anlamlı olarak pozitif korelasyon bulundu.

SONUÇ: Çalışmamızda, ileri yaş, ilk RRT öncesinde yüksek ortalama kan basıncı varlığı, kardiyovasküler hastalık mevcudiyeti, SDBY nedeni olarak diyabetin saptanması, artmış ESH, serum albumin düzeyinin düşüklüğü ve ko-morbid hastalıkların varlığı ile hastaların yaşam süreleri arasında ilişki tespit edildi.

ANAHTAR SÖZCÜKLER: Son dönem böbrek yetmezliği, Renal replasman tedavisi, Diyabet

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INTRODUCTION

The burden of chronic kidney disease (CKD) has been an epidemiological, social and economical problem in both developing and developed countries all over the world. According to World Health Organization (WHO) data urinary tract and kidney diseases cause approximately 850,000 deaths per year and 115,010,117 disability adjusted life years (1). The Third National Health and Nutrition Examination Survey (NHANES III) reported that the prevalence of CKD in the U.S. adult population was estimated to be 10.8% (approximately 19.2 million people) (2). In Turkey increased prevalence and incidence of CKD has become a major cause of death. According to 2008 registry data from Turkish Society of Nephrology, prevalence of end-stage renal disease (ESRD) has doubled while incidence of ESRD has increased nearly four-fold since 2000 (incidence, 52 vs. 188 per million people (pmp); prevalence, 358 vs. 756 pmp, respectively) (3). In Konya, a city of Middle Anatolian region of Turkey, there is an increasing number of patients receiving hemodialysis and peritoneal dialysis. The aim of this study was to investigate the etiologies of ESRD, factors affecting progression to ESRD and mortality rates of patients for the past 5 years in Konya.

MATERIAL and METHODS

Subjects

This is a retrospective and cross-sectional study including 417 end-stage renal disease patients (207 female and 210 male) between 16 and 90 years of age receiving renal replacement therapy (RRT) for the first time in the dialysis unit of Selcuk University, Meram School of Medicine in Konya, Turkey. Patients with acute infection, acute renal failure and malignancy were excluded. The study was approved by the Ethic Committee of Selcuk University Meram School of Medicine, and all participants were examined by an internal medicine specialist having at least five years of experience. Serum samples were collected after 12 hours of fasting and stored at -80 C for testing.

Measurements

Body weight was measured in kilograms by using a digital scale (Tefal Sensio). After measuring body weight and height, BMI was calculated as kg/m². Obesity was defined as BMI \geq 30 kg/m² (4).

Blood pressures of the patients were measured by sphygmomanometer (Erka D-83646 Bad Tölz; Germany) twice after five minutes' rest with five-minute intervals. An average of two measurements was recorded as mmHg. Hypertension was defined as a blood pressure $>140/90$ mmHg (5).

Serum creatinine levels were measured by an automatic device (Hitachi Modular E 170-kit from Roche Diagnostics, Tokyo, Japan) using a modified kinetic Jaffe method.

Fasting blood glucose (FBG) levels were measured by using an automatic device (Hitachi Modular E 170-kit from Roche

Diagnostics, Tokyo, Japan). Diabetes was defined as FBG \geq 126 mg/dL (6).

Measurement of Renal Function and Co-morbidity Index

CKD was defined as kidney damage and/or decreased kidney function expressed as glomerular filtration rate (GFR) for at least 3 months regardless of the cause (7). GFR was calculated by the MDRD formula at the "http://www.hdcn.com/calcf/gfr.htm" website using the serum creatinine value (mg/dL), age (years), gender and race (8).

Co-morbidity was expressed using the Wright-Khan index. This index was developed in 375 dialysis patients followed for at least 2 years and divides the population into three risk levels based on age and the presence of comorbid conditions. These consist of (1) age <70 years with no comorbidity; (2) age 70 – 80 with no comorbidity, or age <70 with diabetes or any age with one comorbidity; and (3) age >80 , or any age with at least two comorbidities, or any age with cardiopulmonary disease or visceral cancer (9-10). According to these parameters low, medium, or high co morbidity were determined in ESRD patients.

Cardiovascular diseases were diagnosed by clinical assessment, ECG and echocardiography in ESRD patients.

Late referral to nephrologist was defined as first nephrology visit <4 months and early referral as first nephrology visit ≥ 4 months prior to initiation of dialysis (11).

Statistical Analysis

Results were expressed as mean \pm SD or rate as percentage. T test was used for comparisons and independent groups, respectively. In addition, Pearson's and Spearman's correlation analyses have been used to detect the associations between GFR and some clinical and demographic parameters. Univariate and multivariate logistic regression analysis were performed to determine any associations between CKD and its risk factors. Logistic regression analysis results were shown with odds ratio (OR) and confidence interval (95% CI), and $p < 0.05$ was considered significant. Statistical analysis was performed by using SPSS version 11.0 (SPSS Inc., Chicago, Illinois, USA).

RESULTS

Demographic and clinical features of the patients are shown in Table I. In this study, 34.3% of patients were over 65 years old and advanced age was found to be a negative prognostic factor on survival in patients with ESRD ($p: 0.0001$). The etiologies of ESRD are shown in Figure 1, symptoms of the patients on admission are shown in Figure 2 and factors affecting survival of patients are shown in Table II.

In the present study we showed that there was an increasing rate of diabetic nephropathy between 2003 and 2004 that was found to be statistically significant in the last two years ($p < 0.005$) (Figure 3). 31.7% of HD patients and 31.5% of CAPD patients had diabetes ($p > 0.05$). We showed that there was a positive

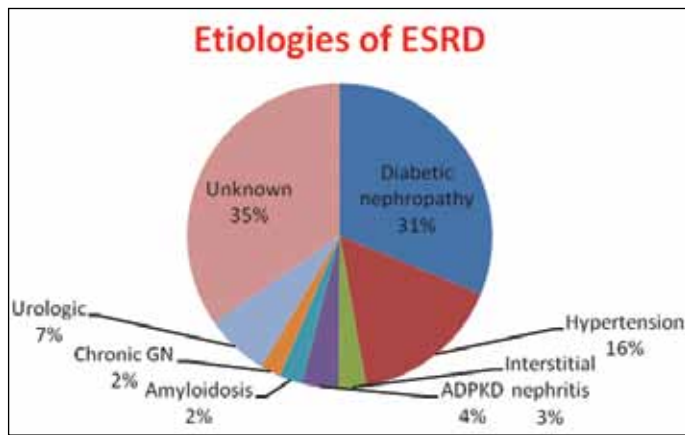


Figure 1: Etiologies of ESRD.

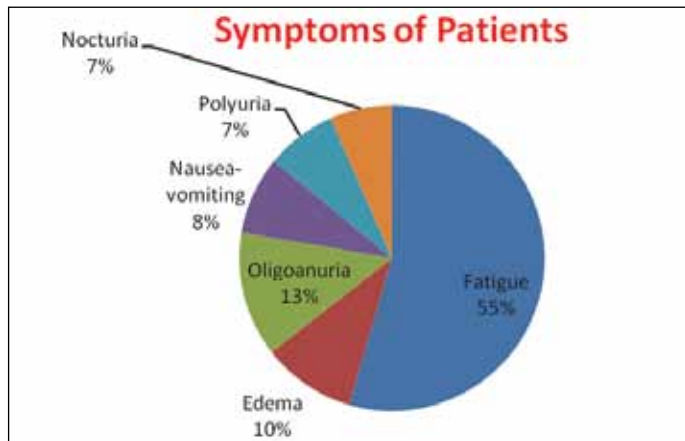


Figure 2: Symptoms of Patients on admission.

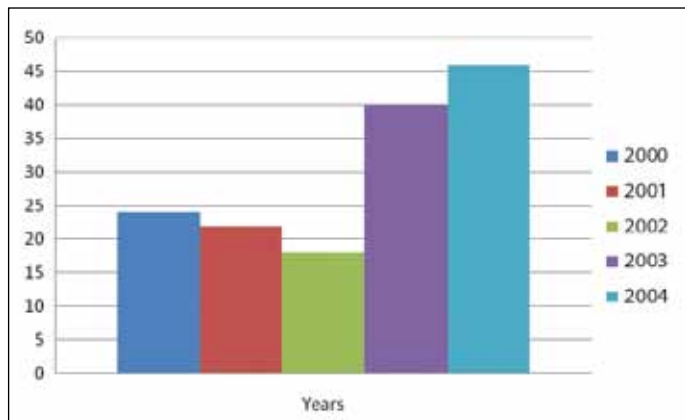


Figure 3: The prevalence of Diabetes in ESRD patients according to years.

correlation between diabetes mellitus and cardiovascular disease in these patients ($r: 0.393, p: 0.0001$).

The present study showed that 68.6% of patients (n: 286) had their first hemodialysis by a hemodialysis catheter, whereas

Table I: Demographic and clinical features of ESRD Patients.

Parameters	Values
Age (years)	55.5 ±15.9
Gender (Female/Male)	207/210
Height (cm) (Female/Male)	157±7/169±7
Weight (kg) (Female/Male)	63.9±16/70±12
Body Mass Index (kg/m ²) (Female/Male)	25.8±5.6/25.3±3.6
Systolic Blood Pressure (mmHg)	143±29
Diastolic Blood Pressure (mmHg)	82±14
Mean Arterial Pressure (mmHg)	102±19
Albumin (g/dL)	3.1±1.2
Smoking Duration and Status of Patients	N
Duration (Years)	29.8±13.5
Package (daily)	1.1±0.4
Non-smokers	303 (72.7%)
Gave up	37 (8.9%)
Smokers	56 (13.4%)
Unknown	21 (5%)
Stage of CKD on Admission	N
Stage 1	7 (1.7%)
Stage 2	37 (8.9%)
Stage 3	63 (15.1%)
Stage 4	82 (19.7%)
Stage 5	228 (54.7%)
First Evaluation of Patients	N
General Practitioner	5 (1.2%)
Internist	190 (45.6%)
Cardiologist	32 (7.7%)
Urologist	25 (6%)
Early referral to Nephrologist	83 (19.9%)
Late referral to Nephrologist	69 (16.5%)
Other	13(3.1%)
The type of Renal Replacement Therapy of Patients	N
HD through A-V Fistula	33 (7.9%)
HD through Jugular Catheter	284 (68.1%)
HD through Femoral Catheter	1 (0.2%)
HD through Subclavian Catheter	1 (0.2%)
PD (Temporarily)	3 (0.7%)
PD (Permanent)	95 (22.8%)

HD; Hemodialysis, **PD;** Peritoneal Dialysis

Table II: Factors affecting survival of patients according to Cox regression analysis.

Factors	Odd ratio (CI 95%)	P Value
Age	1.5	0.0001
Mean BP Before the First Dialysis	0.9	0.01
Diastolic BP Before the First Dialysis	0.9	0.009
Serum Albumin Levels	1.4	0.03
Patients with Cardiovascular Disease	1.7	0.03
Diabetes as an Etiology of ESRD	1.7	0.03
ESR>100 mm/hr	2.2	0.002

BP: Blood Pressure, **ESRD:** End-stage renal disease, **ESR:** Erythrocyte sedimentation rate

31.4% of patients received either hemodialysis through an A-V fistulae or peritoneal dialysis through a permanent peritoneal catheter. Within the first 90 days, the mortality rates of the patients receiving hemodialysis through a catheter and A-V fistula and receiving peritoneal dialysis were 8.9%, 3.6%, and 7.1% respectively. There was a positive correlation between acute dialysis and mortality ($r: 0.140, p: 0.006$).

After the first dialysis session, patients continued hemodialysis (n: 198, 47.4%) and peritoneal dialysis (n: 190, 45.5%). Fourteen patients (3.3%) were switched from hemodialysis to peritoneal dialysis or vice versa. Nine patients (2.2%) underwent renal transplantation and 5 patients (1.2%) survived without any renal replacement therapy.

In the present study, the prevalence of cardiovascular disease (CVD) in patients receiving HD and CAPD was 45.7% and 36%, respectively ($p: 0.04$). One, three and five year survival rates of HD patients were calculated as 74.3%, 62%, and 60%, respectively. In CAPD patients these rates were 86%, 73% and 68% for one, three and five years, respectively. Mean average survival duration of HD and CAPD patients were 39.7 ± 2.1 and 47.1 ± 2.1 months, respectively ($p: 0.0006$). However, according to corrected mortality and survival rates (patients <55 years without CVD and DM), there was no statistically significant difference between HD and CAPD patients ($p > 0.05$). The co-morbid diseases of patients are shown in Figure 4.

In our study, 13.4% of patients were smokers and there was no statistically significant correlation between mortality and smoking ($p > 0.05$).

Patients were classified according to Wright-Khan mortality index (Figure 5). In the low risk group, one-year and five-year survival rates were 96% and 90%, respectively. However, these results were 83.5% and 61% in the moderate risk group, and 63.5% and 44% in the high risk group respectively. The difference in survival rates between the groups was statistically significant ($p: 0.00001$). Mean survival times of patients were

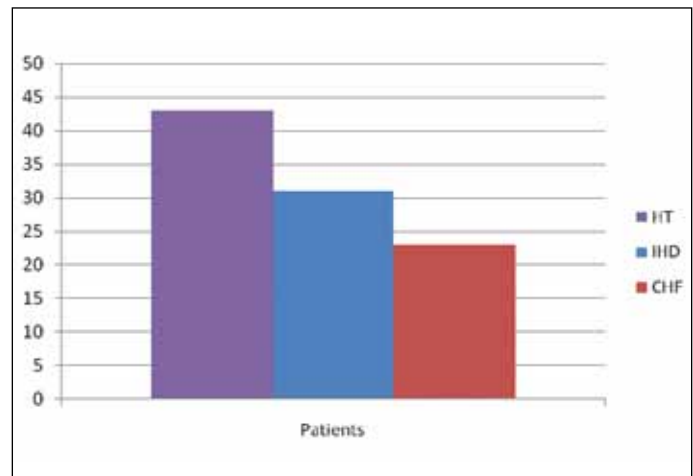


Figure 4: The percentages of co-morbid diseases in ESRD patients. **HT**, hypertension; **IHD**, ischemic heart disease; **CHF**, congestive heart failure

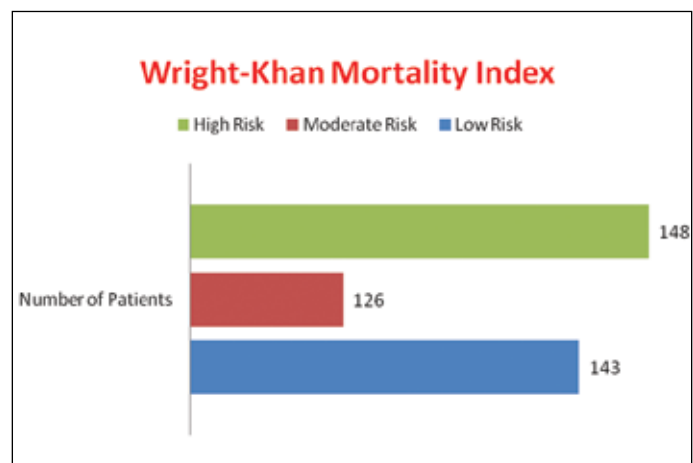


Figure 5: Number of Patients according to the Wright-Khan Mortality Index.

56±1.3, 44.3±2.5 and 29.7±2.4 months, in low, moderate and high risk groups, respectively. When patients were classified according to dialysis modality (Figure 6), the difference between HD and CAPD groups was statistically significant (p: 0.0002).

Time period between diagnosis and starting of RRT was smaller in diabetics when compared with the other groups (p<0.001). The longest period was 73.9 months in the ADPKD patients.

The mean time from diagnosis to starting of dialysis in patients referred to nephrologists early were significantly longer than patients referred late (p: 0.00001). Mortality rates of patients referred to nephrologists and of the other patients were 18.2% and 23.8%, respectively and there was no significant difference between these two groups (p>0.05).

Discussion

The main findings of the present study were as follows:

- i) Advanced age, increased mean arterial BP before the first RRT, having CVD, DM as an etiology of ESRD, increased erythrocyte sedimentation rate (ESR), decreased serum albumin levels, serum urea levels, HD through a catheter for the first time, receiving HD as a continuous RRT, and the presence of co-morbid diseases were found as the factors that affected survival of the patients.
- ii) There was an increasing rate of diabetic nephropathy between 2003 and 2004.
- iii) The time period between diagnosis and starting of RRT was smaller in diabetics and the longest period was 73.9 months in the ADPKD patients.
- iv) We found a statistically significant relationship between acute dialysis and mortality.
- v) The prevalence of cardiovascular disease was found to be higher in HD patients when compared with PD patients. However, one, three and five year survival rates of HD patients were higher than PD patients.
- vi) According to the Wright-Khan mortality index, patients in the low risk group had higher one- and five-year survival rates when compared with patients in the moderate and high risk groups. However, in subgroup analysis, there was no statistically significant difference between HD and CAPD patients.
- vii) Early referral to nephrologist was found to be valuable for patients in terms of late receiving RRT.

The cause of the global burden of CKD can be attributed to increasing life expectancy of patients with chronic diseases such as diabetes, hypertension and cardiovascular disease. Any assessment of CKD predictors is complex, since there is considerable interaction of CKD with race and age, and with other chronic diseases mentioned above. Delayed diagnosis and

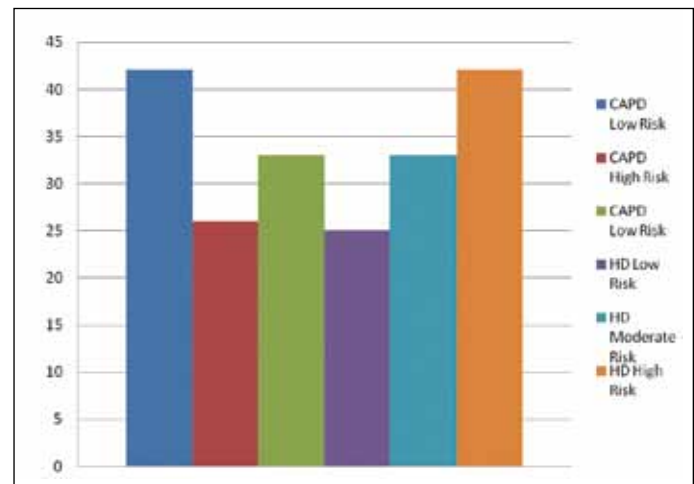


Figure 6: The percentages of HD and CAPD patients according to the Wright-Khan Mortality Index.

failure of institution of measures to slow progression of renal failure is another major problem.

The incidence of ESRD is likely to be higher than that reported in Turkey. However, there are now reliable epidemiologic data about ESRD and related chronic diseases including diabetes, hypertension, dyslipidemia, cardiovascular disease and chronic glomerulonephritis in the renal registry reports of Turkish Society of Nephrology (3).

Diabetes is the most important risk factor for CKD development (12). Diabetes is the most prominent cause of ESRD both in our country and developed countries. In Turkey, 27% of the pre-dialysis population is diabetic (3, 13). Chadban et al. (14) reported that the ratio of patients with GFR < 60 mL/min in the diabetic population was 27.6%. Sahin et al (15). showed that the CKD prevalence in the diabetic population was approximately 1.5–2 times greater than in the non-diabetic population. Similarly, diabetes prevalence in CKD and non-CKD population was 8.06% and 5.11%, respectively. A recent study showed that the overall prevalence of diabetes was 12.7% in Turkish population (16). In our study, the rate of diabetic nephropathy was found to be increased especially in the last two years. The main reasons for the increased rate of diabetic nephropathy might be secondary to increased incidence of obesity, metabolic syndrome, changes in dietary habits and more sedentary lifestyle in our country (16-17).

In a study, Rayner et al. (18) showed that mortality was associated with increasing age, non-black race, coronary artery disease, congestive heart failure, diabetes mellitus, peripheral vascular disease, cerebrovascular disease and smoking in hemodialysis patients. Our findings were partially consistent with this study.

In our study, the one-year mortality rate was found to be 25.7% in HD patients and 14% in CAPD patients. In the United

States, the crude one-year mortality rate of the ESRD patients was 22%, considerably higher than the rate in European DOPPS countries (16%) or Japan (7%). By using Japan as the reference group, the crude RR of mortality was significantly ($P < 0.0001$) greater both in Europe (RR = 3.12) and in the US (RR = 5.34). These statistics showed that mortality varies markedly between regions and those regional differences are considerably, but only partially, reduced after correction for case-mix (19).

In a French study by Chantrel et al. (20) 84 type 2 DM patients entering HD were evaluated regarding survival and its predictors. Almost 80% of patients needed acute HD due to hypervolemia and pulmonary edema (42%) at the beginning of the therapy. Sixty-four percent of these patients were hypertensive in spite of appropriate antihypertensive therapy. After 211 days, 32% of diabetic patients were deceased secondary to CVD. In this study the authors also determined that early referral of patients to nephrologists could improve prognosis (20). Our findings were also consistent with this study. We showed a positive correlation between diabetes mellitus and cardiovascular disease in ESRD patients and mortality rates of patients were found to be worse when compared with patients referred to nephrologist early. We also found that there was a statistically significant relationship between acute dialysis and mortality that can be attributed to the increased CVD risk in ESRD patients.

Vonesh et al. (21) analyzed the data from 398,940 United States Medicare patients initiating dialysis between 1995 and 2000. Of the 398,940 patients studied, 11.6% used PD as initial therapy, 45% had diabetes mellitus (DM), 51% were 65 years or older and 55% had at least one co-morbidity. Among the 178,693 (45%) patients with no baseline co-morbidity, adjusted mortality rates in non-DM patients were significantly higher on HD than on PD. Among diabetic patients with no co-morbidity, HD was associated with a higher risk of death among younger patients and a lower risk of death among older patients. Within the group of 220,247 (55%) patients with baseline co-morbidity, adjusted mortality rates were not different between HD and PD among non-diabetic patients. As a conclusion of this study, survival differences between HD and PD are not constant, but vary substantially according to the underlying cause of ESRD, age, and level of baseline co-morbidity (21). These data were also consistent with our findings.

In our analysis according to the Wright-Khan mortality index, patients in the low risk group had higher one- and five-year survival rates when compared with patients in moderate and high risk groups. However, in subgroup analysis, there was no statistically significant difference between HD and CAPD patients. These results were similar to the study done by Misculin et al. (22). In this study, one year mortality rates were 4.9%, 18.9%, and 31.7% in low, moderate and high risk groups, respectively according to the Wright-Khan mortality index.

Kazmi et al. (11) examined the impact of timing of nephrology care relative to initiation of dialysis on mortality after initiation of dialysis. Among patients with CKD who initiated dialysis, late referral of patients was associated with higher risk of death

at 1 year after initiation of dialysis compared with early referral. In our study, patients referred to nephrologists had a lower mortality rates when compared with other patients. When we compared early and late referred patients to nephrologists as a first step doctor, there was a statistically significant difference between these patients. There was also a statistical significance between two groups for the mortality rates in the first 90 days.

In the present study, patients were classified according to serum albumin levels to assess their nutritional status and there was a statistically significant negative relationship between serum albumin levels and mortality. Iseki et al. (23) also demonstrated that serum albumin levels were the most important determinant of mortality in 1243 ESRD patients.

In conclusion; CKD is a growing health problem worldwide that leads to ESRD. ESRD, diabetes and CVD are the most common cause of morbidity and mortality in the most countries including Turkey. Longitudinal studies are needed to determine cardiovascular outcomes in ESRD patients.

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