ORIGINAL ARTICLE

Comparison of Turkish and US haemodialysis patient mortality rates: an observational cohort study

Gulay Asci[1], Daniele Marcelli[2], Aygul Celtik[1], Aileen Grassmann[2], Kutay Gunestepe[3], Mustafa Yaprak[1], Abdulkerim Furkan Tamer[1], Mehmet Nuri Turan[1], Mehmet Sukru Sever[4] and Ercan Ok[1]

[1]Division of Nephrology, Ege University School of Medicine, Bornova, Izmir, Turkey, [2]Fresenius Medical Care, Bad Homburg, Hessen, Germany, [3]Fresenius Medical Care, Istanbul, Turkey and [4]Division of Nephrology, Istanbul University School of Medicine, Istanbul, Turkey

Correspondence to: Aygul Celtik; E-mail: aygulceltik@gmail.com

Abstract

Background: There are significant differences between countries in the mortality rates of haemodialysis (HD) patients. The extent of these differences and possible contributing factors are worthy of investigation.

Methods: As of March 2009, all patients undergoing HD or haemodiafiltration for >3 months ($n = 4041$) in the Turkish clinics of the NephroCare network were enrolled. Data were prospectively collected for 2 years through the European Clinical Dialysis Database. Mean age ± standard deviation was 58.7 ± 14.7 years, 45.9% were female and 22.9% were diabetic. Comparison with US data was performed by applying an indirect standardization technique, using specific mortality rates for patients on HD by age, gender, race and primary diagnosis as provided by the 2012 US Renal Data System Annual Data Report as reference.

Results: The crude mortality rate in Turkey was 95.1 per 1000 patient-years. Compared with the US reference population, the annual mortality rate for Turkey was significantly lower, irrespective of gender, age and diabetes. After adjustments for age, gender and diabetes, the mortality risk in the Turkish cohort was 50% lower than US whites [95% confidence interval (CI) 0.46–0.54, $P < 0.001$], 44% lower than US African-Americans (95% CI 0.52–0.61, $P < 0.001$) and 20% lower than Asian-Americans (95% CI 0.74–0.86, $P < 0.05$).

Conclusions: The annual mortality rate of prevalent HD patients was found to be significantly lower in the studied Turkish cohort compared with that published by the US Renal Data System Annual Data Report. Differences in practice patterns may contribute to the divergence.

Key words: haemodiafiltration, haemodialysis, mortality, practice patterns, Turkey

Introduction

Despite improvements in dialysis treatment, patients on maintenance haemodialysis (HD) have a markedly higher mortality rate compared with the general population. According to the 2012 US Renal Data System (USRDS) report, the expected life span is 8 years for incident HD patients aged 40–44 years and 4.5 years for those aged 60–64 years [1]. The major cause of death is cardiovascular disease, accounting for 50% of deaths.

There are significant inter-country differences in annual mortality rates of HD patients. The HD patient mortality rate is significantly higher in the USA than in Europe and Japan. This disparity may partially be explained by the differences in mortality rates of the general population in the various countries [2]. Additionally, variations in patient age, prevalence of comorbid diseases, underlying renal disease and racial/genetic status all contribute to survival of dialysis patients [3, 4]. Finally, differences in practice patterns also impact survival rates, e.g. weekly dialysis duration, vascular access type, physician care and management of hypertension, hyperphosphataemia and anaemia [5–11].

The Turkish National Registry reports a crude mortality rate in prevalent HD patients as low as 10.0/100 patient-years [12], although the validity of this low mortality rate might be affected by the retrospective and questionnaire-based nature of the data collection. Another report with higher-quality data obtained from 1074 prevalent HD patients receiving dialysis from a single provider chain in Turkey found a 9.6/100 patient-years crude mortality rate in Turkish prevalent HD patients. Both values are much lower than what is reported for US white patients (23.6/100 patient-years in 2009) and also for European patients (13.3–18.6/100 patient-years) [13–15]. However, it is possible that the low mortality rate observed in Turkish HD patients may be due to the calculation method and has inadequate or no adjustment for gender, age and diabetes. In fact, the Turkish HD population is much younger and has a relatively lower diabetes prevalence compared with US patients [12].

The aim of this study was to determine the mortality rate in a relatively large Turkish HD cohort using prospectively recorded data and to compare the mortality rate adjusted by age, gender, race and diabetes with that of the US HD population, as obtained from the 2012 USRDS annual data report.

Materials and methods

Patients receiving maintenance HD at 41 HD centres operated by Fresenius Medical Care in Turkey were enrolled in this observational cohort study. The study's start date was March 2009, and follow-up time was 2 years. Inclusion criteria were age 18 years and older and initiation of dialysis more than 3 months before baseline (i.e. the study population comprised prevalent dialysis patients only, to facilitate alignment with the US cohort). Baseline and follow-up data, including time of death, were collected from the European Clinical Dialysis Database (EuCliD) in Turkey, which has been validated and used since 2001 [13, 16]. The patients were censored at the time of transfer to other dialysis facilities or to other renal replacement modalities. The data from the patients who transferred to another treatment modality or to other dialysis centres were recorded until premature termination and were included in all analyses.

All patients were dialysed with polysulfone membranes (94% high-flux) and bicarbonate-based dialysate. Dialysate sodium concentration was prescribed as 138 mEq/L in all patients; potassium and calcium concentrations were prescribed according to individual needs.

All biochemical analyses were measured using an Abbott Architect c8000 autoanalyzer (Abbott Diagnostics, Chicago, IL, USA) in the same central laboratory. All blood samples were taken before a mid-week HD session.

All Turkish HD patients were Caucasian.

US mortality data were extracted from the USRDS database, 2012 USRDS Annual Data Report. The USRDS is a national data system that provides information about chronic kidney disease and end-stage renal disease (ESRD) in the USA. A central goal is to describe the prevalence and incidence of ESRD and to provide data sets and samples of national data to support research by other research bodies. The data used in this analysis were provided in Table H.8.1 of the 2012 USRDS Annual Data Report and refer to over 375 000 prevalent HD patients with breakdown information according to age, gender, race and primary diagnosis.

Ethics approval and consent to participate

The study was conducted in accordance with the ethical principles of the Declaration of Helsinki and compliance with Good Clinical Practice Guidelines; all patients provided written informed consent.

Statistical analysis

Comparison between Turkish and US mortality data was performed on the basis of standardized mortality rate (SMR) calculations and by applying the indirect standardization technique, using as reference-specific mortality rates for patients on HD by age, gender, white race and primary diagnosis as provided by Table H.8.1 of the 2012 USRDS Annual Data Report. The following steps were taken during the analysis: (i) for each subgroup that is homogenous in terms of age, gender, race and primary diagnosis, the mortality rate from the USRDS table (per 1000 patient-years) was multiplied by patient time at-risk in the corresponding Turkish cohort. Since a specific Turkish reference population group was not available in the USRDS database, we selected comparisons with US whites, African-Americans and Asian-Americans separately. This yields the expected number of deaths according to USRDS specific mortality rates. (ii) The sum of the observed deaths for the same homogenous subgroups was calculated also in the Turkish cohort. (iii) The SMR was calculated as the ratio of the observed to the expected mortality. Values lower than one mean that the mortality rate in the evaluated population of Turkish patients is lower than that in the US reference population [17].

Statistical significance was defined as P < 0.05. All analyses were performed using SPSS software version 13.0 (SPSS, Inc., Chicago, IL, USA). Data were expressed as mean ± standard deviation.

Results

Baseline characteristics of the Turkish patient cohort 2009–2011

After excluding patients younger than 18 years (n = 17) and those who were on dialysis for <3 months (n = 266), 4041 Turkish patients were entered into the final analysis. Patient characteristics are shown in Table 1. Mean age was 58.7 ± 14.6 years, and median time on HD was 48.2 months. Fifty-five per cent of patients were male. Twenty-five per cent of patients had diabetes.

The primary cause of ESRD was diabetes (22.9%), followed by hypertension (21.1%) and glomerulonephritis (6.7%). Other and unknown causes accounted for 49.3%.

Vascular access was arteriovenous (AV) fistula in 86.1% of the cases. Mean length of sessions was 238 ± 6 min, and mean eKt/V was 1.46 ± 0.23; 90.3% of the patients were predominantly treated with conventional HD (>50% of the sessions during follow-up) and 9.7% were predominantly treated by post-dilution on-line haemodiafiltration.

Hypertension (systolic blood pressure >140 mmHg and/or diastolic blood pressure >90 mmHg) was present in 24.1% of the patients. Approximately 6% of the patients had an interdialytic weight gain (IDWG) of >5.7% (corresponding to 4 kg IDWG in a patient weighing 70 kg).

Overall mortality rate

During 2 years of follow-up, 649 of the 4041 patients died (16.1%), 158 were transplanted (3.9%), and 446 moved to other dialysis modalities or to non-participating HD centres (11.0%).

Table 1. Characteristics of the Turkish cohort 2009–2011 (*n* = 4041) and the US cohort

	Turkish cohort	US cohort
Age (years)	58.7 ± 14.6	58.9
Gender (male, %)	55.0	56.8
Time on HD [months, median (IQR)]	48.2 (23.5–90.2)	
Diabetes (%)	25.3	38.5
Aetiology of ESRD (%)		
Diabetes	22.9	38.5
Hypertension	21.1	25.2
Glomerulonephritis	6.7	14.5
Others	11.5	
Unknown	37.8	
Dialysis type (%)		
HD	90.3	
Haemodiafiltration	9.7	
Dialysis session length (min)	238 ± 6	na
Vascular access (%)		
AV fistula	86.1	55.0
AV graft	3.1	27.2
Permanent catheter	10.8	17.7
Body mass index (kg/m^2)	24.9 ± 4.72	na
Postdialysis body weight (kg)	67.1 ± 13.6	na
IDWG (kg)	2.30 ± 0.91	na
IDWG (% body weight)	3.48 ± 1.38	na
Systolic blood pressure (mmHg)	128.8 ± 18.3	na
Diastolic blood pressure (mmHg)	76.4 ± 8.9	na
Antihypertensive medication (%)	29.7	na
eKt/V	1.46 ± 0.23	na
Creatinine (mg/dL)	7.90 ± 2.00	na
Albumin (g/dL)	4.00 ± 0.31	na
Haemoglobin (g/dL)	11.6 ± 1.3	na
Phosphate (mg/dL)	4.81 ± 1.05	na

IQR, interquartile range; na, data not available in USRDS.

There was no difference in characteristics between the patients who prematurely terminated the study because of transfer to another centre and those who remained in the study. The patients who were transplanted during the study period were younger and had less frequency of diabetes compared with the patients who remained in the study (age: 57.7 ± 14.2 versus 42.3 ± 11.1 years, P < 0.001 and diabetes: 12.7 versus 26.2%, P = 0.04, respectively).

Crude mortality rate was 95.1 per 1000 patient-years. Comparison of specific unadjusted mortality rates of Turkish patients with US patients is reported in Table 2. The Turkish annual mortality rate was significantly lower than that published by the USRDS for the US population, irrespective of gender, age or diabetes.

Crude mortality rates of Turkish and USRDS cohorts and expected mortality rate of the Turkish cohort adjusted by race are displayed in Figure 1. Gender, age group and cause of ESRD in the Turkish cohort were adjusted to the same year cohort of the white, Asian-American and African-American cohorts, respectively. SMRs of the Turkish sample were calculated using USRDS data as reference. After adjustment for age, gender and diabetes, the mortality risk in the Turkish cohort was 50% lower than US white, 44% lower than US African-Americans and 20% lower than Asian-Americans (Table 3).

After exclusion of patients predominantly on haemodiafiltration, the crude mortality rate was still lower in Turkish HD patients than in the US white HD patients (103 per 1000 patient-years). Compared with the US whites, adjusted relative risk for overall mortality was 0.53 (95% confidence interval 0.49–0.57, P < 0.001).

Discussion

The mortality rate of prevalent HD patients was found to be lower in the studied Turkish cohort compared with that published by the USRDS. Racial differences, younger age and lower prevalence of diabetes may be postulated to contribute to this discrepancy. However, in this study, a survival advantage persisted after adjustment for age, race, gender and diabetes such that the mortality risk in the Turkish cohort was 50% lower than US whites, 44% lower than US African-Americans and 20% lower than Asian-Americans. Mortality rates were not different in men and women (58 and 61% relative risk reductions, respectively). Regarding age, the lower mortality rate of Turkish patients was much more prominent in younger patients. The survival advantage observed in this cohort over US patients was blunted in diabetics: risk reduction was 37% in diabetics, while it was 59% in the whole population.

In 2003, DOPPS data reported a crude annual mortality of 6.6, 15.6 and 21.7% in Japan, Europe and the USA, respectively [3]. Some evidence suggests that this is in part due to the country-specific differences in the general population mortality rates (particularly due to cardiovascular disease). However, as the life

Table 2. Raw mortality rate (per 1000 patient-years) comparison by gender, age group and diabetes

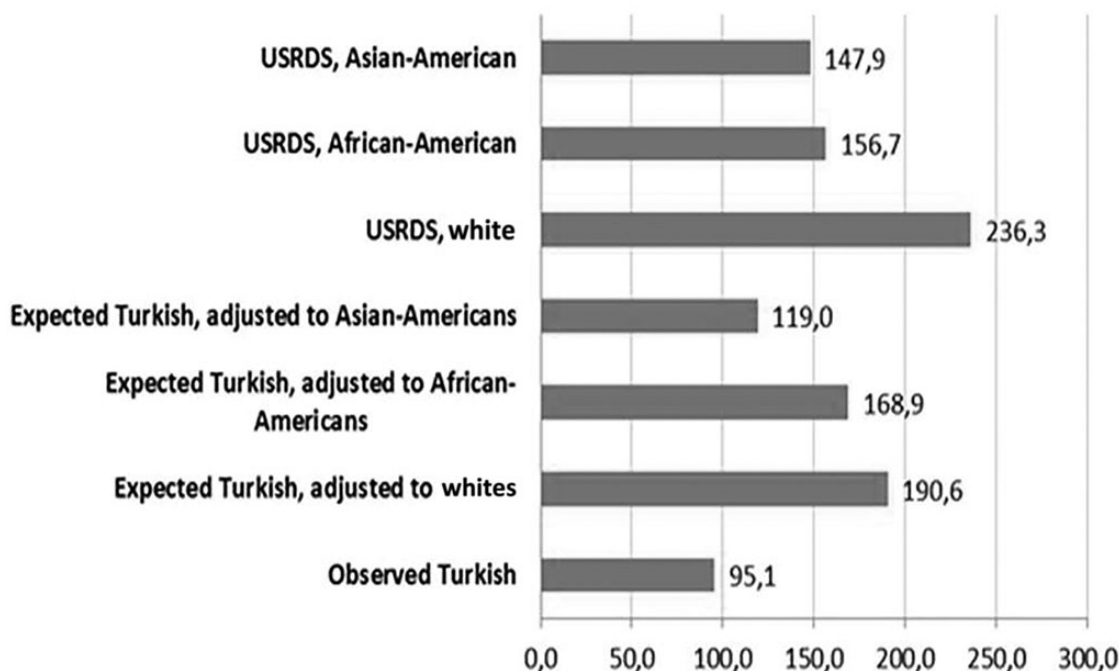|	All	Gender		Diabetes	Age group		
		Female	Male		20–44 years	45–64 years	65+ years
Turkey	95.1	90.4	99.0	154.8	21.6	72.4	164.2
US whites	236.3	234.2	237.9	245.6	75.2	162.9	330.3
RR	0.41	0.39	0.42	0.63	0.29	0.45	0.50

Fig. 1. Crude mortality rates of Turkish and USRDS cohorts and expected mortality rate of the presented cohort adjusted by race. Gender, age group and cause of ESRD in the presented cohort were adjusted to the same year cohort of whites, Asian-Americans and African-Americans, respectively.

Table 3. SMR for the Turkish cohort compared with the USRDS cohort

Reference	Standardized mortality ratio	95% Confidence interval	P-value
US white	0.499	0.461–0.539	<0.001
African-American	0.563	0.520–0.608	<0.001
Asian-American	0.799	0.738–0.863	<0.05

expectancy of the general population in Turkey is lower than in the USA (United Nations World population prospects: 2012 revision), this cannot explain the higher survival we observed in this Turkish cohort of HD patients.

Comparisons of mortality rates in HD patient populations may be flawed by the use of different calculation methods. A recent study, which was similar to ours, compared survival rates in a group of Chinese patients with USRDS data using the same method applied in the USRDS calculations [18]. The annual mortality for Beijing HD patients was found to be lower than that of their USRDS counterparts in adjusted analyses. The authors speculated that differences in race or practice patterns might be responsible for the lower mortality rate in their cohort. In our study, the survival advantage we found for Turkish HD patients was evident in all race groups' comparisons.

Practice patterns differ significantly between countries and could affect outcomes. There was a large difference in the proportion of patients dialysed with AV fistula between the two cohorts, which is associated with better survival rates compared with AV graft or catheter: 86% in this cohort versus 55% in USRDS report [1]. The mean duration of the HD sessions was 238 min in the Turkish cohort, while it is 214 min for the US patients according to

DOPPS data [7]. More strikingly, 33.1% of the sessions in the USA were shorter than 200 min compared with only 0.3% in the Turkish cohort [7]. A 30-min decrease of dialysis session duration from 240 min is associated with a 19% increase in mortality risk, and the relative risk for mortality is 1.34 in patients treated with sessions of duration below 211 min [6], independent of body size [5].

Both hypertension and overhydration, which is the major cause of hypertension, have been found to be independent predictors of mortality in HD patients [19, 20]. Removal of excess volume by appropriate ultrafiltration and strict dietary salt restriction has been shown to normalize blood pressure in the majority of dialysis patients [21]. The prevalence of hypertension is substantially lower in this Turkish cohort (24.1%) compared with the prevalence (69%) reported in DOPPS North America data, probably reflecting better dry weight management in patients [20].

A further difference in practice patterns between Turkey and the USA is the frequency and duration of doctor visits. The presence of a dialysis physician during treatments in HD clinics is obligatory according to Turkish legal regulations. In the USA, HD patients are usually seen by nephrologists weekly or less frequently [8]. A recent DOPPS analysis reported that each 5-min shorter duration of patient–doctor contact was associated with a 5% higher risk for death [8].

This study has several limitations. The major limitation is the lack of comorbidities in survival analyses. The relatively younger age and the lower frequency of diabetes in the Turkish cohort are likely to contribute to the low mortality rate, although the survival advantage persisted even after adjusting for age and diabetes. Lower mortality rates observed in the Turkish cohort were present in also the older age group and the diabetics; however, it was less pronounced in those. Secondly, studying

prevalent patients may result in survivor bias. However, the mean dialysis duration was similar in the Turkish and the US cohorts (4.02 and 4.05 years, respectively). Moreover, a survival advantage of the Turkish cohort was evident in all dialysis vintage groups compared with the US patients (unadjusted mortality rates in Turkish and US patients: <2 years, 111.8 versus 208.8; 2–5 years, 107.3 versus 200.2; >5 years, 78.6 versus 197.3 per 1000 patient-years). The low renal transplantation rate in Turkey compared with the USA may contribute to better survival; as expected, patients transplanted were younger, and the frequency of diabetes was lower. Finally, it is questionable whether the study cohort is representative of the total Turkish HD population. Although demographics and primary diagnosis are very similar to what is reported by the Turkish Registry for the total HD population, treatment characteristics may differ in our study population.

In conclusion, we reported that the annual mortality for the studied Turkish cohort was lower than that of their USRDS counterparts and that this difference persisted after adjusting for baseline demographics. The reason for the significant disparity is unclear, but significant differences in practice patterns may play a contributory role.

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Conflict of interest statement

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