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ORIGINAL ARTICLE

Dialyzing women and men: does it matter? An observational study

Ayse Serra Artan[1], Fatih Kircelli[2], Ercan Ok[3], Murvet Yilmaz[4], Gulay Asci[3], Cengiz Dogan[5], Ozgur Oto[1], Kutay Gunestepe[2], Ali Basci[3] and Mehmet Sukru Sever[1]

[1]Division of Nephrology, Department of Internal Medicine, Istanbul Medical Faculty, Istanbul, Turkey, [2]Fresenius Medical Care, Istanbul, Turkey, [3]Ege Medical Faculty, Izmir, Turkey, [4]Bakirkoy Dr. Sadi Konuk Education and Research Hospital, Istanbul, Turkey and [5]CEND Consulting, Istanbul, Turkey

Correspondence and offprint requests to: Ayse Serra Artan; E-mail: ayseserra@gmail.com

Abstract

Background: Application and consequences of hemodialysis treatment may differ between genders; focusing on these differences may be useful to optimize outcomes.

Methods: Data from 1 999 648 hemodialysis sessions performed in 10 984 (3316 incident and 7668 prevalent) patients, treated in 55 centers of the European Clinical Database (EuCliD)–Turkey, were analyzed, and various demographic, clinical, biochemical, therapeutic and prognostic parameters were compared.

Results: There were 1905 male and 1411 female incident and 4339 male and 3329 female prevalent patients. For females, the mean age in incident (61.8 ± 14.9 years) and prevalent (58.3 ± 15.2 years) patients was higher than for males (60.2 ± 14.8 and 56.5 ± 14.9 years, respectively) ($P < 0.001$ for both analyses). Also, body mass index was higher, while the hemoglobin level, and the percentage of interdialytic weight gain and arteriovenous fistula were lower. Serum phosphorus was similar in both genders in incident cases, while it was lower in prevalent female patients. Serum parathyroid hormone levels were lower in incident, but higher in prevalent male cases. Erythropoiesis-stimulating agents and vitamin D preparations were more frequently used in female incident and prevalent patients. Hospitalization was more frequent in prevalent females, while it did not differ significantly in the incident cases. Overall, no significant difference was observed in survival rates at 3 years in both incident and prevalent male and female patients.

Conclusions: Many parameters differ significantly between female and male dialysis patients. Considering the effects of sex on several parameters may be a valuable approach for achieving better outcomes when formulating treatment strategies in this patient population.

Key words: end-stage renal disease, gender, hemodialysis treatment

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Introduction

The mortality risk in chronic hemodialysis patients is unacceptably high, with a 5-year survival rate of only 36% in incident cases [1]. Since many traits and also comorbidities differ significantly among the patients, individualization of therapy may be useful for improving outcomes. Accordingly, a tailor-made treatment protocol needs to consider gender-related differences, because not only demographic characteristics but also many clinical, laboratory and therapeutic features that may affect morbidity and mortality differ significantly between the two genders.

However, apart from a very recent Dialysis Outcomes and Practice Patterns Study (DOPPS) study [2], no study had been specifically designed to search for sex-related differences in hemodialysis practice; the effects of gender on the dose of hemodialysis, erythropoietin requirements, vascular access and compliance have been reported only in the context of subgroup analyses [3–6]. We therefore analyzed a large cohort of hemodialysis patients in order to investigate the effects of several variations on the outcomes in male and female cases.

Materials and methods

Study population

The European Clinical Database (EuCliD®) collects clinical, laboratory and prognostic parameters of hemodialysis patients who are being dialyzed in various centers of Fresenius Medical Care (FMC) localized in different countries since 2002 [7]. We obtained data on 1 999 648 hemodialysis sessions performed in 10 984 (3316 incident and 7668 prevalent) patients, dialyzed in 55 centers of FMC–Turkey. Patients with acute kidney injury were not included in the study.

Incident patients were defined as those who had started maintenance hemodialysis treatment within the preceding 3 months in an FMC clinic, or in other dialysis centers, but moved to an FMC chain within the study period (between May 2009 and May 2012). Prevalent patients were defined as those receiving chronic hemodialysis for >3 months.

Participants were followed up until death or up to leaving of the FMC clinics for any reason. Thus, follow-up time was censored at the study end for patients who did not leave the facility. With regard to the mortality statistics, the data on patients who died within the first month after leaving the FMC chain were analyzed as well. By using this methodology, the time period when the patients were under observation and 1 month after leaving the FMC chain was included in the survival analyses.

Demographic data were retrieved from the patient files. Information regarding hemodialysis application was entered into the EuCliD database instantly via electronic data input devices (personal digital assistant) and desktop computers by the attending nurses during each hemodialysis session. Laboratory data were imported to EuCliD directly from database of the laboratory service provider via an interface.

Data for the patients who had left FMC clinics were obtained by repeated, various types of communications between the FMC clinics' and new clinics' head nurses.

Measurements

Blood pressure was measured a minimum of five times (before, at hourly intervals and after) in each dialysis session. More frequent measurements were performed in the case of any subjective complaints, symptoms or complications. Monthly blood urea nitrogen, creatinine and potassium levels were measured in both predialysis and postdialysis serum samples. Serum glucose, sodium, calcium, phosphorus, total protein, albumin, alanine aminotransferase levels and hemogram were determined monthly in the predialysis serum specimens. Serum iron, iron binding capacity, ferritin, parathyroid hormone (PTH) and HbA1c levels were measured at 3-monthly intervals. All of the laboratory parameters were determined in four central laboratories, which were registered to several quality-control program audits and are certificated by international agencies at least twice per year.

Outcomes

The odds of achieving many clinical, therapeutic and laboratory targets, hospitalization and the probability of patient survival by gender were evaluated as outcome measures.

Statistical analysis

Descriptive statistics for all numeric variables, including means, standard deviations together with the proportions of all categorical variables, were calculated. Mann–Whitney *U*-test was used when the numeric variables did not distribute normally in the independent two groups. Differences between group proportions were examined by χ^2 analysis.

The probability of patient survival according to gender was estimated using a generalization of the Kaplan–Meier estimates. The survival of the patients who had achieved ideal (reference) targets was then compared with the patients who were characterized by lower or higher values than the reference with Kaplan–Meier log rank test.

The association between gender and mortality was assessed using Cox regression models adjusted for age, body mass index (BMI), and time period with end-stage renal disease and many comorbid conditions {including vascular access [percentage of dialysis sessions performed by using arteriovenous fistula (AVF), arteriovenous graft (AVG), permanent or temporary catheters], dialysis prescriptions [mean treatment time, blood flow, ultrafiltration rate, single pool *Kt*/*V*], hemoglobin, serum albumin, calcium, phosphorus and PTH}.

SPSS 15.0 for Windows was used to conduct the statistical analysis.

Statistical significance was accepted at P-values <0.05.

This study was approved by the Istanbul School of Medicine Clinical Studies Board/Ethics committee (Approval No.: 2014/1391). All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. For this type of study, formal consent is not required.

Results

Incident patients

Demographic features

Overall, there were 3316 incident patients; of these, 1905 were males and 1411 females. The total number of hemodialysis sessions in the incident patients was 399 954. Females underwent 176 142 sessions; this figure was 223 812 for the males.

Males were significantly younger compared with the females, while females had higher BMI values (Table 1). When compared

Table 1. Demographic characteristics, features of hemodialysis practice and laboratory parameters in incident and prevalent male and female patients[a]

	Incident patients			Prevalent patients		
Parameter	Female	Male	P	Female	Male	P
Age (years)	61.8 ± 14.9	60.2 ± 14.8	0.001	58.3 ± 15.2	56.5 ± 14.9	<0.001
BMI (kg/m^2)	26.8 ± 6.2	24.7 ± 4.5	<0.001	25.8 ± 5.6	24.6 ± 4.4	<0.001
Dialysis vintage (months)	0.5 ± 0.9	0.6 ± 0.9	0.6	62.7 ± 54.6	61.6 ± 54.0	0.3
DM (%)	39.8	34.6	0.003	28.5	27.2	0.2
AVF (%)[b]	48.8 ± 44.3	57.5 ± 43.3	<0.001	77.2 ± 37.9	85.4 ± 31.1	<0.001
AVG (%)[b]	1.7 ± 12.0	1.3 ± 10.1	0.08	3.9 ± 17.9	2.0 ± 13.1	<0.001
Untunneled catheter (%)[b]	19.3 ± 34.7	19.1 ± 34.4	0.9	2.0 ± 11.4	1.5 ± 10.4	0.001
Tunneled catheter (%)[b]	27.7 ± 41.2	19.2 ± 35.8	<0.001	12.1 ± 29.9	6.4 ± 22.3	<0.001
Blood flow (mL/min)	296.3 ± 45.8	306.4 ± 45.6	<0.001	319.5 ± 43.3	332.0 ± 41.2	<0.001
Kt/V	1.4 ± 0.3	1.2 ± 0.2	<0.001	1.6 ± 0.3	1.4 ± 0.2	<0.001
Creatinine (mg/dL)	5.83 ± 1.86	6.75 ± 2.31	<0.001	7.13 ± 1.68	8.51 ± 2.25	<0.001
Potassium (mmol/L)	4.77 ± 0.74	4.75 ± 0.72	0.1	5.06 ± 0.62	5.08 ± 0.62	0.4
Albumin (g/dL)	3.68 ± 0.47	3.72 ± 0.49	0.01	3.91 ± 0.32	3.98 ± 0.34	<0.001
Calcium (mg/dL)	8.65 ± 0.70	8.61 ± 0.61	0.02	8.95 ± 0.65	8.93 ± 0.64	0.1
Phosphorus (mg/dL)n	4.56 ± 1.20	4.61 ± 1.21	0.5	4.74 ± 1.10	4.91 ± 1.20	<0.001
PTH (pg/mL)	303.4 ± 247.9	281.5 ± 219.8	0.03	401.5 ± 370.3	429.5 ± 388.8	0.02
Hemoglobin (g/dL)	10.35 ± 1.26	10.71 ± 1.32	<0.001	11.19 ± 1.13	11.68 ± 1.26	<0.001
Ferritin (ng/mL)	688.3 ± 520.2	597.4 ± 440.2	<0.001	905.8 ± 549.1	728.14 ± 527.1	<0.001

BMI, body mass index; DM, diabetes mellitus; AVF, arteriovenous fistula; AVG, arteriovenous graft; PTH, parathyroid hormone.
[a]All laboratory parameters were assessed in predialysis serum samples.
[b]Percentage of dialysis sessions performed by this particular access.

Table 2. Three-year survival rates with regard to several parameters in the incident male and female patients

	P*	<Reference	Reference	>Reference	P**
BMI		<21 kg/m^2 (*n*)	21–25 kg/m^2 (*n*)	>25 kg/m^2 (*n*)	
Female	0.087	56.9% (243)	75.0% (320)	75.8% (735)	0.009
Male	0.001	53.1% (324)	66.1% (689)	73.5% (726)	0.002
IDWG/dry weight		<1.4%	1.4–4.2%	>4.2%	
Female	<0.001	46.8% (188)	75.8% (1012)	65.3% (144)	0.168
Male	<0.001	38.9% (259)	69.6% (1332)	67.8% (213)	0.646
Predialysis systolic BP		<100 mmHg	120–140 mmHg	>200 mmHg	
Female	<0.001	29.5% (39)	72.2% (761)	***(1)	***
Male	<0.001	22.0% (35)	71.5% (1032)	***(0)	***
Kt/V		<1.2	1.2–1.4	>1.4	
Female	<0.001	39.2% (166)	70.9% (409)	76.1% (672)	0.028
Male	<0.001	49.9% (475)	68.9% (922)	74.9% (279)	0.609
Hb		<9 g/dL	11–12 g/dL	>13 g/dL	
Female	***	***(173)	84.9% (394)	***(14)	***
Male	<0.001	29.8% (191)	78.9% (602)	57.3% (55)	0.109
Phosphorus		<3.5 mg/dL	3.5–5.5 mg/dL	>5.5 mg/dL	
Female	<0.001	44.1% (196)	75.8% (865)	65.5% (209)	0.188
Male	<0.001	48.5% (247)	64.6% (1134)	83.3% (337)	0.009
PTH		<130 pg/mL	130–585 pg/mL	>585 pg/mL	
Female	<0.001	59.3% (247)	77.3% (798)	47.6% (110)	0.024
Male	<0.001	59.8% (363)	69.3% (1070)	68.1% (106)	0.943
Albumin		<3.5 g/dL	3.5–4 g/dL	>4 g/dL	
Female	<0.001	16.9% (294)	75.4% (722)	83.3% (253)	0.027
Male	<0.001	37.0% (398)	66.9% (868)	81.6% (454)	0.001

BMI, body mass index; BP, blood pressure; Hb, hemoglobin; PTH, parathyroid hormone, IDWG, interdialytic weight gain.
P*: statistics for comparing lower values than the reference.
P**: statistics for comparing higher values than the reference.
***: statistics unavailable because of insufficient number of patients or a follow-up <3 years.

with the reference values, higher than ideal BMI was associated with better survival in both genders, while lower BMI was associated with a worse survival only in the males (Table 2).

Overall dialysis vintage did not show a difference between males and females. Frequency of diabetic nephropathy was significantly higher among females. The number of patients being

transferred to peritoneal dialysis (PD) was very low; in the incident patients, three females and two males were switched to PD. More [63 (3.3%)] males were transplanted compared with females [23 (1.6%)] (P = 0.003).

Dialysis practice

AVF was the most frequently used vascular access type in both genders; it was even more frequently used in males when compared with females, while tunneled catheter usage was more frequent in females (Table 1).

AVF usage was associated with better survival in both genders when compared with central catheters; however, when compared with AVG as a vascular access, usage of AVF was characterized by better survival in males, but not in females (data not shown).

Interdialytic weight gain (IDWG)/dry weight was 2.7 ± 1.4 and 2.8 ± 1.4% in the females and males, respectively (P = 0.020). An IDWG/dry weight <1.4% was associated with worse survival in both genders; patients with IDGW/dry weight >4.2% were characterized by an unfavorable outcome as well, however, without significance (Table 2). Predialysis systolic (130.6 ± 15.7 versus 126.7 ± 15.4 mmHg) and diastolic (77.6 ± 8.0 versus 76.4 ± 8.1 mmHg) blood pressures were higher (P < 0.001 for both analyses) in males when compared with the females. Lower blood pressures were associated with significantly worse survival in both sexes (Table 2).

Kt/V values were higher in females (Table 1); both male and female patients with lower *Kt/V* values had worse survival when compared with the patients who achieved the target of 1.2. Higher *Kt/V* values were associated with better survival only in females (Table 2).

Laboratory parameters, and erythropoiesis-stimulating agents and vitamin D usage

Laboratory variables in both sexes are shown in Table 1. In the univariate outcome analysis, which compares higher and lower values with the targets, the following findings were noted: males with lower or higher hemoglobin values were characterized by worse survival, although the latter did not reach significance (Table 2). Low phosphorus values were associated with unfavorable survival in both sexes; males, but not females, were characterized by better survival with higher serum phosphorus. Lower and higher PTH values indicated a poor survival in both genders; however, this did not reach significance in male patients with high PTH values. Considering serum albumin, lower values were associated with poor survival in both genders (Table 2).

The percentage of patients who had been prescribed erythropoiesis-stimulating agents (ESAs) was higher in female patients (75.5%) when compared with male patients (73.9%), however without statistical significance (P = 0.305). Of note, despite vitamin D preparations having been prescribed more frequently (43.8 versus 38.2%) (P < 0.001), serum PTH levels were higher in the females. Glycemic control, determined by HbA1c levels, was similar in male (7.7 ± 1.7%) and female (7.7 ± 1.8) cases (P = 0.6).

Hospitalization and survival

Frequency of hospitalization was 33.0% in female patients, while this figure was 32.4% for the male patients (P = 0.7). 295 males and 199 females died among the incident patients, giving rise to mortality rates of 14.1% in female patients and 15.5% in male patients (P = 0.3). Survival rates within the first 3 months did not differ significantly between the two genders (data not provided). One-, two- and three-year survival rates were 84.9, 77.3 and 71.5%, respectively, in the female patients; corresponding figures were 83.1, 76.2 and 65.9% in the males, respectively (P = 0.2) (Figure 1).

The comparison of the survival rates of the male and female incident patients who achieved or did not achieve ideal targets (reference values) for several demographic, clinical, biochemical and therapeutic parameters is shown in Table 2.

In the multivariate analysis, age, tunneled and untunneled catheter usage, BMI, *Kt/V*, blood pump rate, hemoglobin, serum albumin and calcium values were found to be predictors for mortality (Table 3).

Prevalent patients

Demographic features

In total, there were 7668 prevalent patients; of these, 4339 and 3329 were males and females, respectively. The number of hemodialysis sessions performed in these patients was 1 599 694. Males were treated by 880 615 sessions; this figure was 719 079 for the female patients. Similar to the incident cases, female patients were characterized by older age and higher BMI (Table 1). When compared with the reference values, significantly better

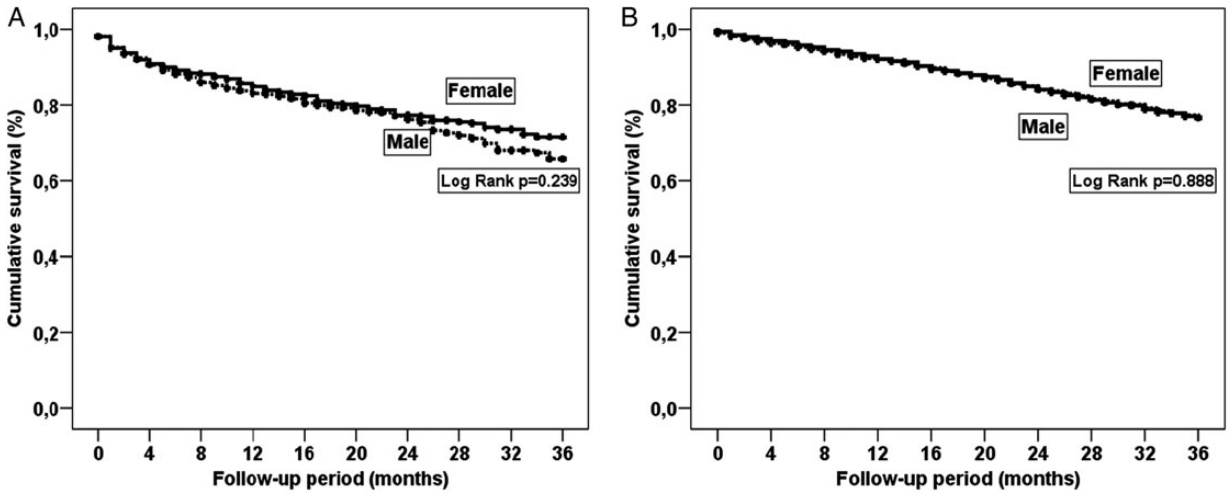

Fig. 1. Three-year survival rates in incident (**A**) and prevalent (**B**) female and male chronic hemodialysis patients.

Table 3. Multivariate analysis of mortality in the incident (A) and prevalent (B) female and male chronic hemodialysis patients

	P	HR	95.0% CI for HR	
(A)				
Age	<0.001	1.028	1.018	1.037
Gender (female)	0.784	1.037	0.802	1.340
Dialysis vintage	0.425	1.051	0.931	1.186
BMI	<0.001	0.943	0.920	0.967
DM	0.852	0.979	0.781	1.227
Vascular access (AVF)	<0.001			
AVG	0.105	1.970	0.869	4.471
Untunneled catheter	<0.001	3.132	2.200	4.459
Tunneled catheter	<0.001	1.854	1.422	2.418
Various vascular access	0.884	1.051	0.543	2.035
eKt/V	<0.001	0.210	0.120	0.368
Blood pump rate	0.034	0.988	0.977	0.999
Processed blood volume	0.172	1.032	0.987	1.079
IDWG/dry weight	0.067	0.000	0.000	1.887
Hemoglobin	<0.001	0.743	0.673	0.820
Albumin	<0.001	0.413	0.312	0.547
Total calcium	0.007	1.343	1.084	1.665
Phosphorus	0.950	1.004	0.895	1.126
iPTH	0.778	1.000	1.000	1.001
(B)				
Age	<0.001	1.037	1.030	1.043
Gender (female)	0.049	1.199	1.001	1.437
Dialysis vintage	0.196	1.001	0.999	1.003
BMI	<0.001	0.928	0.911	0.945
DM	<0.001	1.863	1.615	2.149
Vascular access (AVF)	0.001			
AVG	0.882	0.970	0.654	1.441
Untunneled catheter	<0.001	2.756	1.583	4.796
Tunneled catheter	0.005	1.329	1.091	1.618
Various vascular access	0.916	0.973	0.580	1.632
eKt/V	<0.001	0.219	0.141	0.339
Blood pump rate	0.667	1.002	0.994	1.009
Processed blood volume	0.235	0.982	0.954	1.012
IDWG/dry weight	0.065	1.072	0.996	1.153
Hemoglobin	<0.001	0.820	0.767	0.878
Albumin	<0.001	0.266	0.211	0.336
Total calcium	<0.001	1.559	1.369	1.776
Phosphorus	0.057	0.925	0.854	1.002
iPTH	0.908	1.000	1.000	1.000

BMI, body mass index; AVF, arteriovenous fistula; AVG, arteriovenous graft; IDWG, interdiaytic weight gain; DM, diabetes mellitus; iPTH, intact parathyroid hormone; HR, hazard ratio; CI, confidence interval.

and worse survival rates were noted with higher and lower BMI scores, respectively, in both genders; however, the latter did not reach statistical significance in the females.

Forty percent of the female patients had been on hemodialysis treatment for <1 year; 30% had been receiving dialysis for >36 months. Corresponding figures for the male patients were 43.1 and 27.8%, respectively. Overall dialysis vintage did not reach statistical significance between the genders. There was only one female patient moving to PD modality from hemodialysis, whereas 144 (3.3%) males and 96 (2.9%) females were transplanted (P = 0.278).

Dialysis practice

AVF was used more frequently in males, whereas tunneled and untunneled catheters, and also AVG were used more frequently in females (Table 1). Usage of AVF was associated with more favorable outcome in both genders when compared with central catheters; however, statistical analysis revealed no survival difference in patients who had used AVF or AVG for vascular access (data not shown).

Similar to the incident cases, *Kt/V* was significantly higher in females. In both genders, survival rate decreased with lower (<1.2) *Kt/V*; higher (>1.4) *Kt/V* was associated with better outcome only in the females.

IDWG/dry weight was 3.3 ± 1.4% in the females and 3.4 ± 1.3% in males, respectively (P < 0.001). An IDGW/dry weight <1.7% was associated with worse survival in both genders; a more favorable outcome was noted in the patients with higher than reference values, however without significance (Table 4).

Predialysis systolic (124.2 ± 17.5 versus 131.2 ± 17.3 mmHg) and diastolic (73.5 ± 9.0 versus 76.6 ± 8.5 mmHg) blood pressures were lower in the females when compared with males (P < 0.001 for both analyses). Male patients with systolic blood pressures <100 mmHg were characterized by a significantly worse survival, whereas this was not the case for females.

Laboratory parameters, and ESA and vitamin D usage

Laboratory parameters are shown in Table 1. Univariate outcome statistics revealed the following findings: both genders were characterized by worse survival in patients with hemoglobin values below 9 g/dL. Hemoglobin values >13 g/dL were associated with worse survival in females, but better survival in males, when compared with the cases with hemoglobin between 11 and 12 g/dL. Lower serum phosphorus (<3.5 mg/dL) was associated with worse survival in both genders; males, but not females, were characterized by a better survival with higher serum phosphorus (>5.5 mg/dL). Lower PTH values (<130 pg/mL) were associated with worse survival in both genders. Male patients with higher (>585 pg/mL) PTH values were noted to have better survival. Serum albumin <3.5 g/dL was associated with poor survival in both genders (Table 4).

ESAs were more frequently used in female patients (75.2%) compared with male patients (65.0%) (P < 0.001). The percentage of patients on vitamin D preparations was higher (56.2%) in females as well, when compared with males (51.6%) (P < 0.001).

Hospitalization and survival

Frequency of hospitalization was more frequent in females when compared with males (31.4 versus 27.7%) (P = 0.001). Overall, 575 males and 463 females among the prevalent patients died, giving rise to mortality rates of 13.9% in females and 13.3% in males (P = 0.4). Survival rates within the first 3 months did not differ significantly between the two genders (data not provided).

One-, two- and three-year survival rates (92.2, 84.1 and 76.6%, respectively) for female patients did not differ significantly when compared with the corresponding figures in the males (92.2, 84.0 and 76.7%, respectively) (P = 0.888) (Figure 1). The survival rates, with regard to achievement of several ideal parameters, are shown in Table 4.

In the multivariate analysis, age, IDWG/dry weight, female gender, AVF, tunneled and untunneled catheter usage, BMI, Kt/V, processed blood volume, hemoglobin, serum albumin, phosphorus and calcium predicted mortality (Table 3).

Discussion

In this study, we analyzed incident and prevalent patients separately, because many clinical and laboratory features, as well as morbidity and mortality figures, might have differed significantly among these two patient cohorts. Also, this separate analysis

Table 4. Three-year survival rates with regard to several parameters in the prevalent male and female patients

	P*	<Reference	Reference	>Reference	P**
BMI	P*	<21 kg/m^2 (*n*)	21–25 kg/m^2 (*n*)	>25 kg/m^2 (*n*)	P**
Female	0.210	71.9% (643)	74.4% (895)	79.3% (1673)	0.03
Male	<0.001	68.3% (814)	76.8% (1625)	81.2% (1729)	0.003
IDWG/dry weight		<1.7%	1.7–5.1%	>5.1%	
Female	0.003	69.6% (304)	76.9% (2637)	82.0% (260)	0.1
Male	<0.001	61.6% (302)	77.2% (3433)	84.8% (374)	0.09
Predialysis systolic BP		<100 mmHg	120–140 mmHg	>200 mmHg	
Female	0.755	79.5% (243)	77.4% (1560)	*** (2)	***
Male	0.036	74.2% (139)	78.6% (2281)	*** (6)	***
Kt/V		<1.2	1.2–1.4	>1.4	
Female	<0.001	45.2% (108)	68.9% (665)	79.7% (2109)	<0.001
Male	<0.001	59.3% (460)	77.6% (2033)	79.8% (1146)	0.6
Hb		<9 g/dL	11–12 g/dL	>13 g/dL	
Female	<0.001	61.4% (100)	80.6% (1332)	67.6% (132)	0.02
Male	<0.001	32.2% (87)	79.0% (1515)	86.1% (494)	0.002
Phosphorus		<3.5 mg/dL	3.5-5.5 mg/dL	>5.5 mg/dL	
Female	<0.001	55.9% (292)	77.2% (2047)	83.1% (n: 625)	0.09
Male	<0.001	53.5% (336)	77.5% (2377)	81.6% (1034)	0.02
PTH		<130 pg/mL	130–585 pg/mL	>585 pg/mL	
Female	<0.001	62.0% (355)	78.7% (1851)	81.7% (445)	0.3
Male	<0.001	61.9% (393)	78.4% (2301)	83.8% (643)	0.01
Albumin		<3.5 g/dL	3.5–4 g/dL	>4 g/dL	
Female	<0.001	35.4% (193)	75.6% (1769)	84.3% (989)	<0.001
Male	<0.001	25.1% (239)	73.1% (1764)	86.1% (1747)	<0.001

BMI, body mass index; BP, blood pressure; Hb, hemoglobin; PTH, parathyroid hormone; IDWG, interdiaytic weight gain.
P*: statistics for comparing lower values than the reference.
P**: statistics for comparing higher values than the reference.
***: statistics unavailable because of insufficient number of patients or a follow-up <3 years.

might have provided a clue for observing the evolution in demographic, clinical and laboratory features of chronic hemodialysis patients over time.

When analyzing survival probability, marginal values were used for some parameters at the expense of neglecting a continuum in their range. As an example, for analyzing the association of survival with hemoglobin levels, values of <9, 11–12 and >13 g/dL were used, while statistics for hemoglobin levels of 9–11 or 12–13 g/dL were skipped. The reason for this policy was to exclude the blunting effects of gray-zone values and focusing on the influence of extreme values on the survival.

Female patients were older in both incident and prevalent cases, reflecting the general trend of higher age in female chronic kidney disease patients [8]. Higher mean age in the incident group when compared with prevalent cases clearly shows that the dialysis population is getting older, as already has been described in other countries [9]. On the other hand, this finding may well be due to a selection bias, because prevalent patients are composed of the survivors, whereas elderly patients might have died previously.

Our data show that in both incident and prevalent patients, when compared with the reference values, higher than ideal BMI was associated with better survival in both genders. The association between BMI and prognosis is controversial; a reverse epidemiology may exist [10], and low body weight may be a disadvantage for survival [11]. A 'U-shaped' curve has also been reported in younger dialysis patients, which suggests that low or very high BMI is associated with elevated risk for death [12].

In the present analysis, the frequency of diabetes was higher in the incident (36.8%) when compared with the prevalent (27.7%) cases, possibly because of increasing number of diabetic patients in the general population over time [13], improved life expectancy in diabetic patients [14] and a progressive increase in the aging population, which is associated with a higher risk of type II diabetes [13].

Despite varying statistics among different counties, almost universally, fistula usage is more frequent among males [5, 15], a finding confirmed by this study as well. Difficulties in surgical technique in constructing AVF due to anatomic reasons [16] and more frequent fistula thrombosis due to higher levels of estrogen [17], and unwillingness of the surgeons because of concerns about higher failure rates, may play a role in the lower AVF usage in the females.

Achievement of IDWG of <5.7% of dry weight is associated with improved survival [18–20]. Since there are major barriers such as nonadherence with dietary prescription, application of too short or ineffective dialysis or using high sodium-containing dialysates [20], this target cannot be achieved in many patients. In the present study, in the incident patients, IDWG/dry weight was significantly lower in incident cases when compared with prevalent cases, possibly due to better preserved residual renal function. This parameter was significantly lower in incident and prevalent female patients; the reason for this finding is obscure. In a cross-sectional multicenter comparative study, male sex was found to be an independent predictor for nonadherence to the fluid restriction [6], although this finding is controversial [21].

Considering laboratory parameters, controversy exists on gender association with chronic kidney disease–mineral bone disease parameters. In the present analysis, serum phosphorus control was better in females, probably due to more effective dialysis, which results in greater phosphorus clearance [22], better compliance with diet [23] and/or better adherence to phosphate binders [24]. It has been reported that not only high but also low serum phosphorus levels can be associated with unfavorable

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prognosis [25], while a clear association between hyperphosphatemia and increased cardiovascular disease has not been demonstrated in females [26]. Moreover, in the present analysis, hyperphosphatemia was associated with better survival in prevalent male patients. Hyperparathyroidism is associated with morbidity and mortality in dialysis patients [27]; however, nearly half of dialysis patients cannot achieve KDIGO targets [28]. In the literature, either no difference with regard to gender [28] or more frequent secondary hyperparathyroidism in females [29] has been reported. In the present database, PTH levels of the incident female patients were significantly higher than the males, in accordance with previous reports [29]. However, in the prevalent cohort, males' PTH levels were higher. The reason for this finding is obscure; worse control of phosphorus and less frequent vitamin D usage in men may explain this finding.

Women were more anemic despite more frequent ESA usage, as has been described previously [30]. This finding may just be a reflection of the higher hemoglobin levels in men in the healthy population [31], while blood and iron loss by menstrual periods in women may be a contributing factor as well [4].

This study has several limitations: first, its observational nature does not give the opportunity to investigate the cause and effect relationship. Second, deaths occurring more than 1 month after leaving FMC clinics could not be detected and analyzed. Third, there is a lack of information about the comorbidities, and causes of hospitalizations as well as deaths could not be defined definitely from the present database.

On the other hand, this study has several strengths: (i) it reports the results of clinical and laboratory data, which are based on a large number of hemodialysis sessions performed on >10 000 patients; (ii) all of the laboratory parameters were determined in well-standardized laboratories, having regular quality-control audits and certificated by international agencies, hence, the possibility of laboratory mistakes is negligible; (iii) due to the use of advanced technology when entering clinical and laboratory data, mistakes in data registration should be minimal; and (iv) entered records were checked for the accuracy of the data at different levels in order to further minimize mistakes in such a large database.

To conclude, although several parameters vary significantly, survival rates do not differ significantly in male and female hemodialysis patients. This finding may be due to mutual existence of several favorable and unfavorable confounding prognostic factors in both sexes, which may offset each other, hence, in the end, resulting in an overall nonsignificance. Importantly, this article raises also the question of a unique target for all patients in the various recommendations. Focusing on the correctable parameters in each sex, and individualizing treatment protocols, may improve the ultimate outcome in both female and male hemodialysis patients.

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Conflict of interest statement

F.K. works in Fresenius Medical Care–Turkey. The other authors declare that they have no conflict of interest.

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