

Impact of Major Surgical Operations on Clinical Outcome in Dialysis Patients

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116

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ABSTRACT

Aim: We aimed to study the impact of major surgical procedures on clinical outcome in patients with end-stage kidney disease (ESKD) treated with hemodialysis (HD) or peritoneal dialysis (PD).

Methods: We retrospectively evaluated chart records of all patients on HD and PD who had been treated for at least 3 months at our outpatient clinics between January 1, 2014 and December 31, 2018. In addition to clinical and laboratory parameters, data on all major surgical procedures were recorded.

Results: Among the 202 patients, 133 (66%) were on HD and 69 (34%) on PD. Forty-seven patients (23%) had a major surgical operation. Operations were emergent in 10 patients (21%) and elective in the others (79%). Among the whole study population, 59 patients (29%) died during the study period. The mortality rate was higher in patients who experienced post-operative complications ($P < .001$). Kaplan–Meier analysis revealed that mean (95% CI) survival time in operated patients was 43 months (37-49 months), while it was 49 months (46-52 months) in the others ($P = .023$). Cox regression analyses revealed that age (RR 1.033, 95% CI 1.010-1.057, $P = .005$), diabetes (RR 2.581, 95% CI 1.474-4.521, $P = .001$), pre-operative C-reactive protein level (RR 1.005, 95% CI 1.002-1.007, $P < .0001$) and undergoing a major surgical procedure (RR 1.868, 95% CI 1.068-3.268, $P = .028$) were independent predictors of mortality.

Conclusion: Our study shows that, in addition to age, diabetes, and inflammatory status, undergoing a major surgical procedure is an independent risk factor for mortality in dialysis patients. Proper management of perioperative complications may result in more favorable outcomes in these patients.

Keywords: End-stage kidney disease, peritoneal dialysis, hemodialysis, surgical procedure, mortality

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INTRODUCTION

The availability of better therapeutic options for managing end-stage kidney disease (ESKD) has increased the lifespan of patients with ESKD. Consequently, with the increasing number of ESKD patients, surgical procedures that are closely or remotely related to chronic kidney disease (CKD) are more frequently required than earlier. CKD in the non-surgical setting is an established independent predictor of mortality and cardiovascular events.¹ Likewise, the perioperative management of various surgical procedures in this population is associated

with high morbidity and mortality, mainly as a result of high cardiovascular risks.²⁻⁴

CKD is associated with endothelial dysfunction and inflammation and microvascular abnormalities. Up to 30-50% of prevalent HD patients show elevated serum levels of inflammatory markers, which may be chronic or acute depending on the various causes.

Inflammatory markers are powerful predictors of mortality, after adjustment for other risk factors. Inflammation



is also responsible for other mortality risk factors such as anemia, malnutrition, vascular disease, and left ventricular hypertrophy.^{5,6} Additionally, major surgical trauma is associated with augmented immune response.⁷

According to the United States Renal Data System Reports, the mortality rate among dialysis patients was 165 per 1000 patient-years in 2017⁸; in Europe, according to the European Renal Association – European Dialysis and Transplant Association (ERA-EDTA) Registry, the one-year survival probability of patients on dialysis is 83.5%.⁹ In 2018, the crude mortality rate for patients on dialysis in Turkey was 143 per 1000 patient-years.¹⁰ However, the contribution of probable adverse effects of major surgical procedures toward the mortality rates of patients on dialysis is not clear.

The present study aimed to investigate the impact of major surgical operations on clinical outcome and risk factors for mortality in dialysis patients.

MATERIALS AND METHODS

This single-center retrospective study was approved by the ethics committee of the institution where the study was conducted (Approval number: I1-66-20). In keeping with institutional procedures, written informed consent was obtained from all the patients at the time of starting dialysis procedures. We included all adult ESKD patients on dialysis who had been treated for at least 3 months at our outpatient clinics between January 1, 2014 and December 31, 2018. We recorded all major operations conducted under general anesthesia, with the exception of renal transplantation. There were 34 patients who underwent transplantation during the study period; however, we did not include those patients in the study. Additionally, we recorded all causes of death, regardless of whether or not they were possibly related to the operation. Electronic medical records were used to obtain medical history and discharge summaries. We noted the patient demographic characteristics, Charlson comorbidity index,¹¹ surgery types, mortality rates, duration of period until death of patient or end of the study, type of dialysis, dialysis vintage, and dialysis modality at the time of surgery. Postoperative complications were noted as

arrhythmias, hypervolemia, hypotension, bleeding, acute myocardial infarction, respiratory failure, and cerebrovascular accident.

In operated patients, pre-operative laboratory results were recorded to investigate whether they were risk factors for mortality. The last available laboratory results were recorded for the patients who were not operated on. Surgeries that were routinely scheduled were referred to as “elective surgeries”, whereas those that were performed as soon as possible after the decision to operate was taken were called “emergent.”

If there was specific information regarding changes in dialysis characteristics in patients’ records, such as the transition to HD or manual exchange for peritoneal dialysis (PD) patients, additional HD sessions, or HD without anticoagulation, it was recorded. General institutional policy for dialysis support in surgical patients was as follows: performing an HD session the night before or on the morning of surgery to prevent fluid and/or an electrolyte imbalance in the immediate postoperative period in HD patients; performing PD the night before surgery and taking the patients to the operation room without fluid in their abdomen; and resuming the PD the day after the surgery unless there was an emergent need for dialysis.

Follow-up time was determined as the time passed between the date of the beginning of the study and either the date of death or that of the end of follow-up (December 31, 2018).

Statistical Analysis

Clinical and laboratory data were expressed as percentage, mean (\pm standard deviation (SD)) or median [interquartile range (IQR)] values, as appropriate. In order to investigate the differences regarding surgery, death, and dialysis modality, the patients were grouped into “operated patients,” “non-operated patients,” “mortality (+),” “mortality (–),” “hemodialysis,” and “PD.” Demographic characteristics, follow-up times and dialysis vintages, and laboratory characteristics were compared between each group. Continuous variables were compared by the *t*-test or Mann–Whitney *U* test, and categorical variables were compared using Pearson’s chi-square or Fischer exact tests. In order to determine the risk factors for mortality in patients, multivariate logistic regression analysis was conducted. Parameters with a *P*-value $<.1$ in univariate analysis were considered for entry in the multiple logistic regression model. The quality of adjustment of the model was tested with the Hosmer–Lemeshow statistic. Odds ratios were expressed with 95% CI. Multivariate cox regression analysis was performed to determine the independent predictors of mortality. Hazard ratios were expressed with 95% CI. The Kaplan–Meier method was used for survival analysis. A threshold value of *P* $<.05$ was considered as statistically significant. The calculations were made with Statistical Package for the Social Sciences (SPSS) version 25.0 (IBM SPSS Corp.; Armonk, NY, USA).

Main Points

- Chronic kidney disease is associated with high morbidity and mortality, mainly as a result of high cardiovascular risks, in both surgical and non-surgical settings.
- End-stage kidney disease patients need surgical procedures for various reasons, with greater frequency than earlier. This increases the importance of proper perioperative surgical management.
- Undergoing a major surgical procedure is an independent risk factor for mortality in dialysis patients, along with other factors of advanced age, inflammatory status, and diabetes mellitus.

RESULTS

Among the 202 patients, 133 (66%) were on HD and 69 (34%) on PD. The mean age (\pm SD) was 58.3 ± 14.5 years, 48% were female and 28% had diabetes mellitus. Ninety-nine patients (49%) started dialysis during the study period (incident dialysis patients). The median dialysis vintage was 52.2 (min-max, 3-228) months and the median follow-up time was 37 (min-max, 1-60) months.

During the study period, 47 patients (23%) had a major surgical procedure. Table 1 shows the comparisons between the operated and non-operated patients. Operations were emergent in 10 patients (21%) and elective in the others (79%). The operation types were cardiovascular in 14 patients, orthopedic in 11, gastrointestinal in 8, genitourinary in 6, parathyroidectomy in 5, and brain, pulmonary, and breast in 1 patient each. Twenty-three of the operated patients died, and the mortality rate was significantly higher than that of non-operated patients ($P=.002$). Severe postoperative complications (arrhythmia, hypervolemia, hypotension, bleeding, acute coronary syndrome, respiratory failure, and cerebrovascular accident) were recorded in 17 (36%) of the operated patients, of whom 16 died. Laboratory results revealed that in operated patients, white blood cell count and serum C-reactive protein (CRP) levels were higher while platelet count and serum uric acid levels were lower, in comparison with the non-operated patients.

Out of the whole study population, 59 patients (29%) died during the study period. Table 2 compares clinical features by mortality. The patients who died were older and had a higher median comorbidity index ($P < .001$). There were no differences regarding dialysis modality. Of the 59 patients who died, 23 (11%) had undergone a surgery. This rate was higher than that for patients who survived. Sixteen (8%) of these 23 deaths occurred within 30 days of the postoperative period. Although it did not reach a significant level, the mortality rate tended to be higher after emergent operations than it was after elective operations. The mortality rate was higher in patients who experienced postoperative complications ($P < .001$). Serum albumin and uric acid levels were lower while serum CRP, ferritin, and white blood cell count were significantly higher in patients who died, compared to those who survived (Table 2).

Table 3 shows the characteristics of the patients regarding dialysis modality. The incidences of having a major surgical operation, postoperative complication, and mortality rate were similar in both groups. In patients who had surgery, 1 PD patient needed transition to HD because of hypervolemia, 1 was a PD patient who performed automated PD at homemade manual exchanges, 3 HD patients needed additional HD sessions, and 10 patients had HD sessions without anticoagulation during the perioperative period.

Multivariate cox regression analysis was conducted in order to determine the predictors of mortality in all participants in the

study. It was revealed that age (RR 1.033, 95% CI 1.010-1.057, $P=.005$), diabetes (RR 2.581, 95% CI 1.474-4.521, $P=.001$), pre-operative CRP level (RR 1.005, 95% CI 1.002-1.007, $P<.0001$), and having a major surgical procedure (RR 1.868, 95% CI 1.068-3.268, $P=.028$) were the independent predictors of mortality (Table 4).

HD patients were followed for a median of 43 months (IQR: 16.2-60) and PD patients were followed for a median of 32 months (IQR: 12.2-52.5). As revealed in the Kaplan-Meier analysis (Figure 1), mean survival time in operated patients was 43 months (95% CI 37-49 months), while it was 49 months (95% CI 46-52 months) in the others ($P=.023$). Fifteen out of 23 deaths (65%) among the operated patients occurred in the first month after surgery.

DISCUSSION

In this single-center retrospective study of 202 dialysis patients (133 HD and 69 PD), we found that over a median duration of 3 years, 23% of the patients had undergone a major surgical procedure and 29% had died. Together with age, diabetes, inflammation, and having a major surgical procedure were found to be independent risk factors for mortality.

Although the prevalence of dialysis patients has decreased over the years, their quality of life, mortality rates, and healthcare utilization are still matters of concern. In 2017, the crude prevalence for ESKD was 2204 per million in the US population⁸, while it was 778 per million in Turkey.¹⁰ Overall mortality is known to be higher among patients on dialysis than in the overall patient population (134 vs. 8.65 per 1000 patient-years).⁸ As already stated, the crude death rate for dialysis patients is higher in the United States than in Turkey (165 vs. 143 per 1000 patient-years). Healthcare utilization capacities, ethnic differences, and effects of the aging population might be the underlying reasons for this discrepancy between countries. With regard to perioperative mortality, the mortality rate is found to be much higher in patients on dialysis. In their cohort of 40 004 patients, who underwent non-cardiac surgery, Spence et al. reported a lower risk of mortality (1.8%) within 30 days after surgery. In that study, only 4.1% of the patients had an estimated glomerular filtration rate of <30 mL/min/1.73 m²; however the number of patients on dialysis was not specified.¹² Drolet et al.¹³ found that patients on dialysis had an increased risk of mortality (22.1%) in their study that analyzed colorectal surgeries. In-hospital mortality after cardiac operations in dialysis patients was found to be higher (15.3%) in Leontyev et al.'s study as well.¹⁴

The possible reason for a higher mortality rate in our study (48.9%) may be the fact that we have included all types of major surgeries during a relatively longer follow-up period.

Although there are conflicting data regarding the mortality by dialysis modality,¹⁵ Kumar et al.¹⁴ showed that 2-year survival after cardiac surgery in HD and PD patients was similar (69%

Table 1. Comparisons Between the Operated and Non-operated Patients

Parameter	Operation (+)	Operation (-)	P
Patients (n)	47	155	-
Age (mean ± SD)	56.83 ± 13.3	58.8 ± 14.9	.39
Female/male	19-40%/28-59.5%	78-50.3%/77-50.7%	.248
Comorbidity score (median, min-max)	5 (2-12)	5 (2-10)	.37
Operation type (emergent/elective)	10/37 (21.2%)	N/A	
Operation type (n, %)		N/A	
CVS	14 (29.7%)		
Orthopedic S.	11 (23.4%)		
GIS	8 (17%)		
GUS	6 (12.7%)		
Parathyroidectomy	5 (10.6%)		
CNS	1 (2.1%)		
Thoracic S.	1 (2.1%)		
Breast S.	1 (2.1%)		
Dialysis vintage (months) (median, min-max)	75 (4-209)	46 (3-228)	.001
Follow-up time (months, [IQR])	43 (22-60)	34 (13.5-60)	.156
Mortality (n, %)	23 (48.9%)	36 (23.2%)	.002
Postop. complication (n,%)	17 (36.1%)	N/A	
Arrhythmias	4		
Hypervolemia	2		
Hypotension	2		
Bleeding	4		
MI	1		
Respiratory failure	2		
CVA	2		
BUN (mean ± SD)	57.1 ± 25.89	59.6 ± 18.7	.319
Creatinine (mean ± SD)	8.1 ± 2.69	7.94 ± 2.93	.434
Sodium (mean ± SD)	137.2 ± 4.04	137.6 ± 3.5	.841
Potassium (mean ± SD)	4.71 ± 0.94	4.78 ± 0.89	.434
Calcium (mean ± SD)	8.9 ± 0.7	8.8 ± 0.8	.624
Phosphorus (mean ± SD)	4.87 ± 1.85	5.15 ± 1.31	.136
Parathyroid hormone (mean ± SD)	571.9 ± 532.8	380.7 ± 325.9	.056
Albumin (mean ± SD)	4.2 ± 5.5	3.5 ± 0.6	.651
Hemoglobin (mean ± SD)	10.7 ± 1.5	10.8 ± 1.7	.9
White blood cell count (mean ± SD)	9.39 ± 3.9	7.7 ± 3.02	.005
Platelet count (mean ± SD)	280 ± 89	236 ± 102	.005
Transferrin saturation (mean ± SD)	26.5 ± 22.1	25.9 ± 13.5	.14
Ferritin (mean ± SD)	582.7 ± 778.6	437.8 ± 741.1	.092
CRP (mean ± SD)	50.3 ± 67.3	30.8 ± 63.7	.002
Uric acid (mean ± SD)	5.59 ± 1.73	6.09 ± 1.26	.034
Bicarbonate (mean ± SD)	21.2 ± 2.7	22.9 ± 20.8	.968

BUN, blood urea nitrogen; CNS, central nervous system surgery; CRP, C-reactive protein; CVA, cerebrovascular accident; CVS, cardiovascular surgery; GIS, gastrointestinal surgery; GUS, genitourinary surgery; IQR, interquartile range; MI, myocardial infarction; S., Surgery; SD, standard deviation.

Table 2. Clinical Features by Mortality

Parameter	Mortality (+)	Mortality (–)	P
Patients (n)	59	143	-
Age (mean ± SD)	65.1 ± 12.5	55.5 ± 14.4	<.001
Female/male	23/36	74/69	.122
Comorbidity score (median, min–max)	6 (2-12)	4 (2-9)	<.001
Cause of death (n)		N/A	-
Arrhythmias	6		
Sepsis	19		
MI	17		
Respiratory failure	4		
CVA	7		
PTE	4		
Traffic accident	2		
Diabetes mellitus (n, %)	25, 42%	31, 21%	.005
Dialysis modality (PD/HD)	18/41	51/92	.518
Dialysis vintage (months)	59.6 ± 41.7	64.0 ± 56.1	.812
Follow-up time (months [IQR])	22 (11-37)	51 (20.5-60)	<.001
Operation (n, %)	23, 38.9%	24, 16.1%	.002
Operation type (emergent/elective)	7/16	3/21	.168
CVS (n, %)	10, 43.4%	4, 16.6%	.06
Postop. Complication (n, %)	16, 69.5%	1, 4.1%	<.001
BUN (mean ± SD)	55.3 ± 23.8	60.6 ± 18.9	.081
Creatinine (mean ± SD)	7.18 ± 2.91	8.33 ± 2.8	.008
Sodium (mean ± SD)	137 ± 4.5	137.7 ± 3.21	.409
Potassium (mean ± SD)	4.56 ± 0.83	4.85 ± 0.91	.409
Calcium (mean ± SD)	8.7 ± 0.96	8.9 ± 0.7	.241
Phosphorus (mean ± SD)	4.97 ± 1.65	5.14 ± 1.36	.276
Parathyroid hormone (mean ± SD)	412.3 ± 451.3	428.7 ± 362.5	.141
Albumin (mean ± SD)	3.1 ± 0.8	3.66 ± 0.48	<.001
Hemoglobin (mean ± SD)	10.6 ± 1.9	10.9 ± 1.6	.263
White blood cell count (mean ± SD)	9.2 ± 4.6	7.7 ± 2.4	.024
Platelet count (mean ± SD)	231 ± 114	253 ± 94	.196
Transferrin saturation (mean ± SD)	27.6 ± 22.3	25.4 ± 12.3	.281
Ferritin (mean ± SD)	789.3 ± 1137	339.5 ± 457	<.001
CRP (mean ± SD)	75.3 ± 97.8	18.6 ± 33.1	<.001
Uric acid (mean ± SD)	5.59 ± 1.57	6.1 ± 1.2	.004
Bicarbonate (mean ± SD)	25.4 ± 3,5	21.4 ± 2.6	.828

BUN, blood urea nitrogen; CRP, C-reactive protein; CVA, cerebrovascular accident; CVS, cardiovascular surgery; HD, hemodialysis; IQR, interquartile range; MI, myocardial infarction; PD, peritoneal dialysis; PTE, pulmonary thromboembolism; Postop., postoperative; SD, standard deviation.

Table 3. Clinical Features by Dialysis Modality

Parameter	Hemodialysis	Peritoneal Dialysis	P
Patients (n)	133	69	-
Age (mean ± SD)	60.8 ± 14.3	53.5 ± 13.8	.001
Female/Male	62/71	35/34	.002
Comorbidity score (median, min-max)	5.23 (2-12)	4.21 ± 1.7 (2-12)	.002
Diabetes mellitus (±)	36	20	.448
Dialysis vintage (months)	70.34 ± 57.2	48.2 ± 37.4	.001
Follow-up time (months [IQR])	43 (16.2-60)	32 (12.2-52.5)	.04
Vascular access		N/A	N/A
Fistula (n, %)	115, 86.4%		
Catheter (n, %)	18, 13.5%		
Ultrafiltration rate (mean ± SD) (mL/day)	2319 ± 944	1741 ± 794	<.0001
Operation (n)	32	15	.427
Operation type (n, emergent/elective)	8 / 24	2/13	.307
CVS (n)	8	6	.238
Mortality (n)	41 (30,8%)	18 (26%)	.297
Postop. complication (n)	12	5	.524
Arrhythmias	1	-	
Hypervolemia	1	1	
Hypotension	2	-	
Bleeding	2	-	
MI	1	1	
Respiratory failure	3	3	
CVA	2	-	
Kt/V (mean ± SD)	1.65 ± 0.37	2.24 ± 0.47	NA
URR (mean ± SD)	74.37 ± 6.1	NA	NA
BUN (mean ± SD)	60.1 ± 21.4	57 ± 18.7	.311
Creatinine (mean ± SD)	7.66 ± 2.7	8.65 ± 2.99	.20
Sodium (mean ± SD)	138.1 ± 3.2	136.2 ± 3.9	<.001
Potassium (mean ± SD)	5.0 ± 0.86	4.27 ± 0.75	<.001
Calcium (mean ± SD)	8.9 ± 0.78	8.77 ± 0.86	.188
Phosphorus (mean ± SD)	5.08 ± 1.44	5.11 ± 1.49	.912
Albumin (mean ± SD)	3.86 ± 3.28	3.37 ± 0.62	.219
Hemoglobin (mean ± SD)	10.8 ± 1.74	10.84 ± 1.64	.879
White blood cell count (mean ± SD)	7.64 ± 3.02	9.15 ± 3.63	.002
Platelet count (mean ± SD)	229 ± 98.3	281.1 ± 98.2	<.001
Transferrin saturation (mean ± SD)	27.2 ± 18	23.7 ± 10.4	.08
Preop. ferritin (mean ± SD)	540.8 ± 814	338.3 ± 595	.07
Parathyroid hormone (mean ± SD)	368.5 ± 345.27	528.2 ± 445	.006
CRP (mean ± SD)	38.9 ± 68.8	28.3 ± 56.7	.27
Uric acid (mean ± SD)	5.79 ± 1.36	6.34 ± 1.39	.008
Bicarbonate (mean ± SD)	20.68 ± 2.77	26.28 ± 31.3	.048

BUN, blood urea nitrogen; CNS, central nervous system surgery; CVA, cerebrovascular accident; CRP, C-reactive protein; CVS, cardiovascular surgery; GIS, gastrointestinal surgery; GUS, genitourinary surgery; IQR, interquartile range; MI, myocardial infarction; SD, standard deviation; URR, urea reduction ratio.

Table 4. Multivariate Cox Regression Analysis Results for Survival

Independent Predictors of Mortality	ExpB	Standard Error	P	HR	95% CI for HR	
					Lower	Upper
Age	0.033	0.012	.005	1.033	1.010	1.057
Diabetes	0.948	0.286	.001	2.581	1.474	4.521
Operation	0.625	0.285	.028	1.868	1.068	3.268
CRP	0.005	0.001	.0001	1.005	1.002	1.007
Albumin	0.003	0.037	.929	1.003	0.934	1.078

CRP, C-reactive protein; OR, odds ratio.

for PD and 66% for HD), which is comparable to our results. Additionally, as in our results, postoperative complication rates were similar in PD and HD as well.¹⁶

122 We found that serum potassium level was higher in HD patients than in PD patients. Although both hyper- and hypokalemia are well-known risk factors for sudden cardiac death in dialysis patients,¹⁷ mortality was not different between the 2 groups of patients in our study, despite the difference in potassium levels.

Although impaired renal function is known to be a risk factor for increased adverse events and mortality in the periprocedural setting, there is no specific recommendation for the dialysis population according to current surgical guidelines.^{18,19} During the perioperative period of patients on dialysis, volume overload, electrolyte disorders, and susceptibility to bleeding deserve tremendous attention.²⁰ Cardiac arrhythmias and sepsis are the most common causes of perioperative mortality in this population.²¹ Likewise, there were more frequent postoperative complications in patients who died in our study population. In order to minimize these complications, the nephrology

department should be consulted before and after the surgery, the correct time of dialysis and surgery should be scheduled, and the patient should be adequately dialyzed, be euvolemic, and have no electrolyte imbalance before undergoing surgery.²⁰

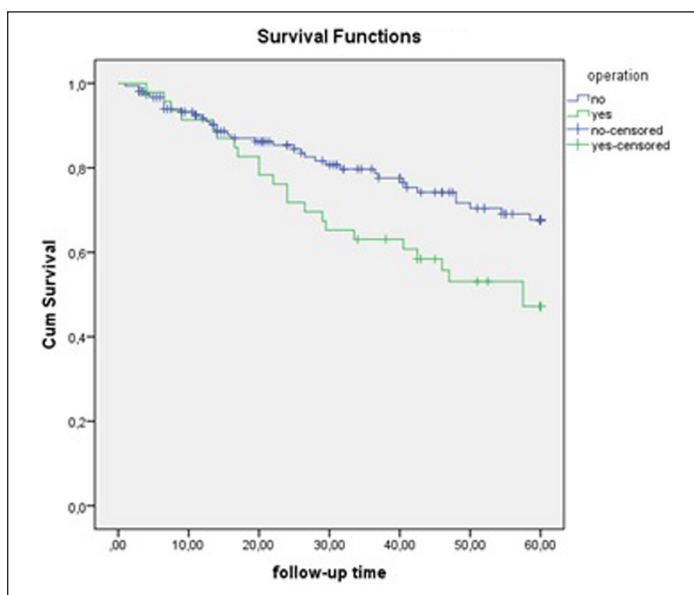
In terms of risk factors, diabetes mellitus and advanced age predict mortality in surgical dialysis patients.²² Emergent surgery is associated with a 5-fold greater risk of death.^{23,24} In all patients, we found that increased age, diabetes, and having undergone an operation are the independent risk factors for mortality. Although it did not reach a significant level, probably due to the limited number of patients in our study, the mortality rate tended to be higher after emergent operations than that after elective operations. Additionally, major surgical trauma is associated with immune response.⁷ These findings are in line with our results which show that inflammation is both a risk factor and a predictor of mortality.

There are several limitations of our study. First, this study has a retrospective design. Second, despite including all PD and HD patients treated within the last 5 years at our center, the number of patients remained relatively low. Third, we included all major surgical operations in the study in order to reveal all the relevant operational risks of dialysis patients; however, this is a confounding factor as well, because not all the operations have the same risks of mortality or complication.

In conclusion, although prospective studies with a higher number of patients are needed to confirm the results, our study shows that in addition to age, diabetes, and inflammatory status, having undergone a major surgical operation is yet another independent risk factor for mortality in patients on dialysis. Prevention and proper management of perioperative complications may result in more favorable outcomes in these patients.

Ethics Committee Approval: Ethics committee approval was received from the Ethics Committee for Clinical Studies of Ankara University School of Medicine (Approval number: I1-66-20).

Informed Consent: Not applicable, due to the retrospective design of this study.

**Figure 1.** Kaplan–Meier survival analysis.

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