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Original Article

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Starting of Renal Replacement Treatment: Two Years Experience

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Abstract

Objective: It is still unclear which parameters will be used when starting renal replacement therapies (RRT) in end stage kidney disease patients. We planned this retrospective study to determine the eGFR in the transition to RRT in our patient population and the RRT preferences with laboratory values.
Materials and Methods: We data from patients who transferred to RRT from low-clearance polyclinic between 2016 and 2017.
Results: 57 patients underwent hemodialysis (HD), 13 patients peritoneal dialysis (PD) and 24 patients preemptive kidney transplantation. In the middle age group (56-75 years), HD was more preferred then preemptive kidney transplantation (p=0.02). In the transition to RRT median eGFR is 8.3 (6.7-9.6) mL/min/1.73 m^2. A statistically significant difference was found between eGFR values when starting different RRTs (p= 0.005). The median eGFRs for HD is 7.4 (5.9-9) mL/min/1.73 m^2, for PD 8.6 mL/min/1.73 m^2 (7.9-10.6), for transplantation 9.3 (7.25-11.2) mL/min/1.73 m^2. This difference was between preemptive transplantation and HD.
Conclusion: It is not appropriate to decide the RRT with a single assessment other than acute complications. Prolongation of the stage 5 chronic kidney disease follow-up may imply postponement of the cost of other high-cost RRTs.
Keywords: End stage kidney disease, renal replacement treatment, timing

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INTRODUCTION

The decision on which parameters to start to renal replacement therapies (RRTs) in patients with end-stage renal disease (ESRD) has changed over the years and is still uncertain. The European Renal Best Practice 2011 (1) and Canadian Kidney Foundation 2014 (2) guidelines determined the estimated glomerular filtration rate (eGFR) as 6 mL/min/1.73 m^2 for initiating to RRT, even if the patient had no complaints. The 2012 Kidney Disease: Improving Global Outcomes (3) stated the GFR limit as 5-9 mL/min/1.73 m^2 whereas. The Japanese Nephrology Dialysis Therapy (4) guideline was set as 2 mL/min/1.73 m^2 for initiating the RRT (2C).

Early initiation of dialysis may expose patients with ESRD to dialysis-related complications earlier (5). Reduction in residual renal function may progress rapidly after dialysis, particularly with hemodialysis (HD) (6). Peritoneal access sites, catheter or bloodstream infections associated with early dialysis may increase in ESRD patients (7).

Most eGFR equations are based on serum creatinine levels, so there is a high likelihood of predicting a higher eGFR at a lower serum creatinine levels due to low muscle mass or excessive fluid overload (8). The dialysis decision, which is now accepted worldwide, accepts

the approach that evaluates the health status of the patient as a whole, including age, gender, physical activity, and comorbidities, rather than only with eGFR. Based on this information, the present study was planned retrospectively for the evaluation of eGFRs, laboratory values, and drugs used and for the determination of RRT preferences in the transition to RRT in our own patient population in the last 2 years.

MATERIALS AND METHODS

In our low-clearance outpatient clinic at the Nephrology Outpatient Clinic, when the patients are diagnosed with stage 4-5 chronic kidney disease (CKD) (eGFR≤30 mL/min/1.73 m^2), a file is opened by the education nurse. After obtaining information about the patient (socioeconomic–cultural), the entire training plan, including the RRT choices, and additional trainings, if necessary, are provided. The patient is referred to the dietician to explain the special diet. Improvable factors, such as anemia, bone mineral metabolism disorder, acidosis, hyperlipidemia, proteinuria, and hypertension, are intervened in our outpatient clinic. Patients with stage 5 CKD (eGFR≤15 mL/min/1.73 m^2) are followed up monthly. This period may vary weekly or biweekly in some patients or cases of acute kidney disease on CKD. With these follow-ups, it can be determined whether the change in the patient's renal function tests is decreased, increased, or in a stable nature. The patient is informed about emergencies requiring RRT. The patient's decision to start RRT is made by the doctor evaluating the clinical and laboratory results together. RRT is initiated in many cases, such as hypervolemia, resistant hypertension, nausea, vomiting, and anorexia. Regular blood pressure was considered as ≤140/80 mm Hg. In the present study, the data of patients who were followed up in the low-clearance outpatient clinic of the Nephrology Polyclinic and started to RRT between 2016 and 2017 were used. This study was conducted retrospectively after obtaining permission (no. 70904504, dated 07/13/2018) from the ethics committee of our university. Informed consent is not necessary due to the retrospective nature of this study.

Statistical Analysis

The Statistical Packages for the Social Sciences (SPSS) version 23 (IBM Corp., Armonk, NY, USA) was used for statistical analysis. Descriptive statistics were presented as frequency, percentage, average±standard deviation, median, first quarter, and third quarter values according to suitability. The assumption of normality was checked by Shapiro–Wilk test, q–q graph, skewness, and kurtosis values. Differences between the two independent groups were evaluated by Student's t for normally distributed variables and Mann–Whitney U test for non-normally distributed parametric variables. Homogeneity of variance was evaluated according to Levene test result in two independent samples t-test. Welch test was used when variance homogeneity was not obtained. Paired t-test was used when for normally distributed variables between the two dependent measurements, and Wilcoxon paired test for non-normally distributed variables and Kruskal–Wallis test was used to compare groups of more than two for non-normally distributed variables. For significant differences, the Bonferroni–Dunn procedure was used in binary comparisons. A chi-square test was used for categorical values. If necessary, post-hoc Pearson chi-square test and Bonferroni correction were performed. A $p<0.05$ was considered statistically significant.

RESULTS

60 patients in 2016 and 43 patients in 2017 were out of follow-up from the low-clearance clinic. Of these 103 patients, 9 (8.7%) died, and 94 (91.3%) passed to RRT. The median age of the 103 patients was 59 (45-68) years. There were 66 (64%) male patients and 37 (36%) female patients. Seven patients died during the stage 5 CKD follow-up. Seven of the nine patients died due to cardiac reasons, one died due to pneumonia, and one died after aortic aneurysm operation.

The number of male patients (62 patients, 66%) at the time of transition to RRT was approximately twice that of female patients (32 patients, 34%). Of these, 57 patients (61%) (19 female and 38 male) started hemodialysis (HD); 13 patients (14%) (5 female and 8 male) started peritoneal dialysis (PD), and 24 patients (25%) (8 female and 16 male) had preemptive kidney transplantation.

The median age of the 94 patients was 57 (42.8-67) years. The number of patients aged >65 years was 27 (28.7%), and the number of patients aged <65 years was 67 (71.3%).

The etiology of CKD is shown in Table 1.

Table 2 shows the distribution of RRT preferences by gender, blood group, and age ranges.

Table 1. Etiology of CKD in the study population

Etiologies	n (%)
Diabetes mellitus	25 (26.5)
Unknown	17 (18)
Glomerulonephritis	14 (14.9)
Hypertension	9 (9.6)
Nephrolithiasis	7 (7.4)
Solitary kidney	5 (5.3)
Polycystic kidney disease	5 (5.3)
Vesicoureteral reflux	4 (4.3)
ANCA-associated vasculitis	2 (2.1)
Analgesic nephropathy	2 (2.1)
Cyclosporine nephropathy	2 (2.1)
After chemotherapy	1 (1)
Familial tubulointerstitial nephritis	1 (1)

Table 2. Distribution of RRT preferences according to gender, blood group, and age

	Hemodialysis n (%)	Peritoneal dialysis n (%)	Preemptive kidney transplantation n (%)	p
Gender				
Female	19 (20.2)	5 (5.3)	8 (8.5)	0.937
Male	38 (40.4)	8 (8.5)	16 (17)	
Total	57	13	24	
Blood type				
O	18 (21.7)	4 (4.8)	5 (6)	0.679
A	20 (24.1)	5 (5.3)	14 (16.9)	
B	5 (5.3)	2 (2.4)	3 (3.6)	
AB	5 (5.3)	0	2 (2.4)	
Age range				
18-35	6 (6.3)	1 (1)	8 (8.5)	0.002
36-55	12 (12.7)	7 (7.4)	11 (11.7)	
56-75	36 (38.3)[a]	5 (5.3)	5 (5.3)[a]	
76-90	3 (3)	0	0	

[a]p<0.004 when the hemodialysis and transplantation groups are compared.

Table 3. Patients' blood clearance at the entry and exit of the low-clearance polyclinic

	Entry	Discharge	p
GFR (mL/min/1.73 m^2) Median (Q1 and Q3)	18.8 (14.27-23.75)	8.3 (6.67-9.6)	<0.001
Hemoglobin (g/dL) Average±standard deviation	11.4±1.6	10.4±1.5	<0.001
Albumin (g/dL) Median (Q1 and Q3)	4.01 (3.7-4.32)	3.9 (3.4-4.2)	<0.001
Calcium (mg/dL) Median (Q1 and Q3)	9.1 (8.7-9.52)	9 (8.27-9.6)	0.278
Phosphorus (mg/dL) Median (Q1 and Q3)	4.2 (3.7-4.72)	5.35 (4.77-6.3)	<0.001
Uric acid (mg/dL) Median (Q1 and Q3)	6.5 (5.5-7.5)	6.65 (5.6-7.72)	0.164
Parathyroid hormone (pg/mL) Median (Q1 and Q3)	171.5 (103-276)	214.5 (109.5-402.2)	0.008

RRT preferences were not different according to gender (p=0.937). There was no statistically significant difference between the blood groups that we thought could affect renal transplantation status (p=0.679). A statistically significant difference was found with respect to age groups and RRT preference (p=0.002). This difference was between HD and transplantation group in 56–75 years old.

Table 4. Follow-up time as stage 5 CKD and transition to RRT according to RRT selections

	Hemodialysis (median, Q1–Q3)	Peritoneal dialysis	Preemptive kidney transplant	p
Stage 5 CKD follow-up period	10 (6-14)	7 (4.5-17)	6.5 (4-9)	0.176
GFR value in transition to RRT (mL/min/1.73 m^2)	7.4 (5.9-9)[a]	8.6 (7.9-10.6)	9.35 (7.25-11.2)a	0.005

[a]When the hemodialysis and transplantation groups are compared.

Table 3 shows the blood values at the admission and discharge of the patients at the low-clearance outpatient clinic.

Ten (9.7%) patients were taken to follow-up at stage 3 CKD, 66 (64%) patients at stage 4 CKD, and 27 (26%) patients at stage 5 CKD. Eighty-nine (94.7%) of the 94 patients had hypertension. Blood pressure control was achieved in than half of the patients (53.2%). Diabetes mellitus was diagnosed in 31 (33%) of the 94 patients.

The median follow-up (time elapsed since the first admission) of the 94 patients at the low-clearance outpatient clinic was 15 (8-33) months. The median duration of stage 5 CKD follow-up was 8.5 (4-14) months. The median eGFR at the time of transition to RRT was 8.3 (6.7-9.6) mL/min/1.73 m^2.

In Table IV, follow-up time as stage 5 CKD and transition to RRT according to RRT selections are given. There was no difference between stage 5 CKD follow-up and RRT preferences (p=0.176). There was a statistically significant difference between RRT preferences and GFR values when they started these choices (p=0.005). This difference was between patients undergoing preemptive kidney transplantation and entering HD, and patients with HD started HD at slightly lower GFR values.

Forty-three patients had arteriovenous (AV) fistula. The median follow-up period was 5.5 (2-12) months. The rate of entering HD from the fistula was 72% among our patients who preferred HD. Seven out of 13 patients who underwent PD had undergone PD changes 14 days after catheter insertion, four patients 20 days later, one patient 60 days later, and one patient 120 days later.

In Table 5, the drugs used by patients at admission and at the time of discharge from low-clearance outpatient clinic are shown.

Table 5. Drugs used by patients at admission and after discharge from low-clearance outpatient clinic

	No. of patients on medication during admission to low-clearance polyclinic n (%)	No. of patients on medication after discharge from low-clearance polyclinic n (%)
Calcium channel blocker	50 (49)	69 (67)
Renin–angiotensin system blocker	45 (44)	15 (15)
Diuretic	38 (37)	47 (46)
Non-dihydropyridine calcium channel blocker	20 (19)	24 (23)
Beta blocker	34 (33)	46 (45)
Alpha blocker	23 (22)	32 (31)
Active vitamin D	46 (45)	73 (71)
Phosphorus connector	40 (39)	64 (62)
Sodium hydrogen carbonate	58 (56)	75 (73)
Erythropoiesis-stimulating agents	12 (12)	35 (34)
Statin	19 (18)	34 (33)
Allopurinol	42 (41)	57 (55)
Polystyrene sulfonate calcium salt	36 (35)	34 (33)

Table 6. The comparison of stage 5 CKD follow-up and protein/creatinine ratio in spot urine

	Stage 5 CKD follow-up period (months) Median (Q1–Q3)		
Protein/creatinine in spot urine (g/gkr)			
1 g/gkr	10.5	2.75-25.5	0.001
1.1-3.5 g/gkr	12[a]	7-16	
3.6 g/gkr	6[a]	4-8	

[a]1.1-3.5 g/gkr compared with the nephrotic level proteinuria group.

While 45 (44%) patients used the renin–angiotensin system (RAS) blocker at the time of admission to the low-clearance outpatient clinic, 30 patients discontinued RAS blockade at discharge. There was a significant relationship between dietary compliance and diuretic use (p=0.041), and 35 patients with good dietary compliance did not use diuretics.

Of our patients, 42.6% had proteinuria at the nephrotic level. The comparison of the duration of follow-up of patients with proteinuria and stage 5 CKD is given in Table 6. Patients with proteinuria at the nephrotic level had a significantly shorter follow-up of stage 5 CKD (p=0.001).

DISCUSSION

In our predialysis outpatient clinic, the number of patients who underwent HD during the transition to RRT in the last 2 years (57) was higher than those who underwent PD (13) and preemptive renal transplantation (24). The median of eGFR in the transition to RRT was 8.3 (6.7-9.6) mL/min/1.73 m^2. It was 7.4 (5.9-9) mL/min/1.73 m^2 for HD, 8.6 (7.9-10.6) mL/min/1.73 m^2 for PD, and 9.35 (7.25-11.2) mL/min/1.73 m^2 for preemptive renal transplantation. There was a statistically significant difference between the HD and preemptive kidney transplantation groups. GFR being higher in kidney transplantation was an expected situation. Although there was no statistically significant difference in our patient groups, preemptive renal transplantation was preferred more in the 18-35 age group, and HD was preferred more in the 56-75 age group. The preference of renal transplantation in the younger age group was an expected outcome. The fistula was formed for the second time in a patient who came to our outpatient clinic because the fistula previously formed in another center did not work. There was no primary fistula dysfunction. Two patients had preemptive renal transplantation with actively functioning fistula. (The fistulas were opened at that time while these patients were being followed up at another center.) A patient who was planned to start PD had to switch to HD because the PD catheter did not work well when it was inserted. After insertion of a peritoneal catheter in one patient, inguinal hernia developed. PD was continued after the operation of hernia with undergoing HD.

There was no difference between the RRT preferences and stage 5 CKD follow-up period. This may be an indicator that all patients have the same close follow-up during stage 5 CKD. While 45 patients used RAS blockers at the admission to the low-clearance clinic, 30 patients discontinued RAS blockade when starting to RRT. This abandonment was due to increased creatinine and/or hyperkalemia. Especially in proteinuric patients, care was taken to maintain to continue RAS blockade.

Some observational studies to date have found an increase in the risk of death (5, 9-17) with the initiation of early dialysis treatment, whereas no difference was found in some (18) or positive effect on survival was detected (19-21) in some other studies. The disadvantages of the studies showing positive effects were that they contained limited or no information about the factors that could affect the timing of dialysis dialysis onset, critical predialysis factors (nephrology care, comorbidity, and general causes), and reasons for early-onset (acute kidney disease, frequent hospitalization, and exacerbations of congestive heart failure) and post-dialysis morbidity and mortality (22).

The only randomized controlled study showing the effects of dialysis timing on survival is the Initiating Dialysis Early and Late (IDEAL) study conducted by Cooper et al. in 2010 (23). In their

study, a total of 828 patients were randomized, and when calculated according to the Cockcroft–Gault formula, if the eGFR value was 10-14 mL/min/1.73 m^2, it was planned to start dialysis as the early onset group; if the value was 5-7 mL/min/1.73 m^2, the dialysis was planned as the late onset group. At the end of the median follow-up period of 3.59 years, there was no difference between the groups with respect to survival and incidence of adverse events (cardiovascular events, infection, or complications). Even if the target was 5-7 mL/min/1.73 m^2 in the late onset group, the eGFRs calculated by the average Modification of Diet in Renal Disease (MDRD) were 7.2 mL/min/1.73 m^2 and 9.0 mL/min/1.73 in the late onset and the early onset groups, respectively. These values indicate that the actual difference in eGFR between the two groups is only approximately 2 ml/min/1.73 m^2. The patients in the late dialysis group started dialysis after an average of 6 months compared with the patients in the early onset dialysis group. However, the IDEAL study reported that the patients in that study were young, well nourished, and better prepared for ESRD and less in need of transient dialysis catheter access. Sixty percent of the patient group, 70% of whom were Caucasian, started RRT with PD. Unfortunately, the relationship between low eGFR (<7 mL/min/1.73 m^2) and mortality to initiate dialysis could not be fully evaluated in this study. The results of the IDEAL study indicated that early dialysis initiation is not unconditionally beneficial for patients with ESRD, and that late initiation strategy may delay the initiation of dialysis for some of the well-prepared patients. Since the IDEAL study represents only a certain population, it may not be correct to generalize the results to all patient populations prepared for dialysis.

According to the Turkey Statistical Institute, the elderly population (aged ≥65 years) in Turkey in 2013 was 5,891,694 people, whereas in the last 5 years, it increased by 17% where it reached up to 6,895,385 people in 2017. While the ratio of the elderly population in the total population was 7.7% in 2013, it increased to 8.5% in 2017. The average life expectancy of a person who reaches the age of 65 years in our country was detected to be 17.8 years. It was observed that this period was 16.1 years for males and 19.3 years for females (24). According to the Joint Report of the T.C. Ministry of Health and the Turkish Nephrology Society Registry System in 2016, patients over the age of 65 years compose 47.7% of all patients undergoing HD initially (25). In light of this information, the patient group over the age of 65 years is among patients who need more attention in our country. In our patient group, 27 (28.7%) patients were aged >65 years, and 67 (71.3%) patients were aged <65 years. In one of the studies showing the slow progression of CKD in elderly patients, 116 patients with CKD were retrospectively analyzed. In this study, a slower progression was observed in CKD progression as age progressed, and it was found that the group with the smallest change was between aged 76 and 87 years (26). In another study in which 461 patients with CKD were examined retrospectively, a very low probability of progression was shown for patients at CKD stage 3 and aged ≥65 years when there was no apparent proteinuria (27). When deciding to start RRT in elderly patients, the slow progression in CKD should be taken into consideration, and the quality of life and life expectancy of these patients should be considered. After starting chronic dialysis, elderly patients are at risk for poor outcomes, particularly cognitive dysfunction, comorbidities, and ischemic cardiovascular diseases (13, 28-34). For these reasons, especially this group of patients needs to be followed up more carefully and treated with care in the transition to RRT. The current EQUAL trial will prospectively try to evaluate 3500 patients who are stage 4 patients with CKD in Europe with over the age of 65 years to death or at the end of the 4-year follow-up period for the initiation of RRT (35). It is also known that patients who are elderly, male, and diabetics and who have low body mass index, high comorbidity with cardiovascular complications, or high dysfunction are likely to start dialysis earlier (12, 36-38). In such patients, it would be appropriate to make the transition to RRT without delay.

The decision of initiating RRT should be made by their nephrologist who is familiar with the patient's past and new conditions and who can evaluate the general condition and course of the patient comparatively. It is not appropriate to decide the chronic dialysis with a single laboratuary assessment of the patient especicially for elder patients, except for acute complications. Extending the follow-up period of patients with stage 5 CKD may mean delaying the cost of HD, PD, or kidney transplantation, which have high costs.

CONCLUSION

One of the main goals of the predialysis outpatient clinic is to protect patients from situations requiring RRT. Patients who were referred early to nephrologists may be followed closely by nephrologists to reasonably extend the transition time to RRT. This may reduce the cost of patients with ESRD. It is among the most important tasks of the low-clearance outpatient polyclinic to direct the patient to regular follow-up (mapping of vessels for HD, maturation of AV fistula, and insertion of PD catheter for PD) at the appropriate time, taking into consideration the accompanying diseases. In our low-clearance outpatient clinic, transition of patients with ESRD to RRTs, neither late nor early- at the most appropriate time- should be among in our goals.

Ethics Committee Approval: Ethics Committee approval was received for this study from the Ethics Committee of Akdeniz University School of Medicine (Number: 70904504/317 13/7/2018).

Informed Consent: Informed consent is not necessary due to the retrospective nature of this study.

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REFERENCES

1. Tattersall J, Dekker F, Heimbürger O, Jager KJ, Lameire N, Lindley E, et al. When to start dialysis: updated guidance following publication of the initiating dialysis early and late (IDEAL) study. Nephrol Dial Transpl 2011; 26: 2082-6. [CrossRef]
2. Nesrallah GE, Mustafa RA, Clark WF, Bass A, Barnieh L, Hemmelgarn BR, et al. Canadian Society of Nephrology 2014 clinical practice guideline for timing the initiation of chronic dialysis. CMAJ 2014; 186: 112-7. [CrossRef]
3. Stevens PE, Levin A; Kidney disease: improving global outcomes chronic kidney disease guideline development work group members. Evaluation and management of chronic kidney disease: synopsis of the kidney disease: improving global outcomes 2012 clinical practice guideline. Ann Intern Med 2013; 158: 825-30. [CrossRef]
4. Watanabe Y, Yamagata K, Nishi S, Hirakata H, Hanafusa N, Saito C, et al. Japanese society for dialysis therapy clinical guideline for "hemodialysis initiation for maintenance hemodialysis". Ther Apher Dial 2015; 1: 93-107. [CrossRef]
5. Wright S, Klausner D, Baird B, Williams ME, Steinman T, Tang H, et al. Timing of dialysis initiation and survival in ESRD. Clin J Am Soc Nephrol 2010; 5: 1828-35. [CrossRef]
6. Jansen MA, Hart AAM, Korevaar JC, Dekker FW, Boeschoten EW, Krediet RT. Predictors of the rate of decline of residual renal function in incident dialysis patients. Kidney Int 2002; 62: 1046-53. [CrossRef]
7. Nguyen DB, Lessa FC, Belflower R, Mu Y, Wise M, Nadle J, et al. Invasive methicillin-resistant staphylococcus aureus infections among patients on chronic dialysis in the United States, 2005-2011. Clin Infect Dis 2013; 57: 1393-400. [CrossRef]
8. Leurs P, Machowska A, Lindholm B. Timing of dialysis initiation: When to start? Which treatment? J Ren Nutr 2015; 25: 238-41. [CrossRef]
9. Crews DC, Scialla JJ, Ebony Boulware L, Navaneethan SD, Nally JV Jr, Liu X, et al. Comparative effectiveness of early versus conventional timing of dialysis initiation in advanced CKD. Am J Kidney Dis 2014; 63: 806-15. [CrossRef]
10. Beddhu S, Samore MH, Roberts MS, Stoddard GJ, Ramkumar N, Pappas LM, et al. Impact of timing of initiation of dialysis on mortality. J Am Soc Nephrol 2003; 14: 2305-12. [CrossRef]
11. Sawhney S, Djurdjev O, Simpson K, Macleod A, Levin A. Survival and dialysis initiation: comparing British, Columbia and Scotland registries. Nephrol Dial Transplant 2009; 24: 3186-92. [CrossRef]
12. Lassalle M, Labeeuw M, Frimat L, Villar E, Joyeux V, Couchoud C, et al. Age and comorbidity may explain the paradoxical association of an early dialysis start with poor survival. Kidney Int 2010; 77: 700-7. [CrossRef]
13. Rosansky SJ, Eggers P, Jackson K, Glassock R, Clark WF. Early start of hemodialysis may be harmful. Arch Intern Med 2011; 171: 396-403. [CrossRef]
14. Evans M, Tettamanti G, Nyrén O, Bellocco R, Fored CM, Elinder CG. No survival benefit from early-start dialysis in a population-based, inception cohort study of Swedish patients with chronic kidney disease. J Intern Med 2011; 269: 289-98. [CrossRef]
15. Bao Y, Dalrymple L, Chertow GM, Kaysen GA, Johansen KL. Frailty, dialysis initiation, and mortality in end-stagerenal disease. Arch Intern Med 2012; 172: 1071-7. [CrossRef]
16. Wilson B, Harwood L, Locking-Cusolito H, Chen SJ, Heidenheim P, Craik D, et al. Optimal timing of initiation of chronic hemodialysis? Hemodial Int 2007; 11: 263-9. [CrossRef]
17. Traynor JP, Simpson K, Geddes CC, Deighan CJ, Fox JG. Early initiation of dialysis fails to prolong survival in patients with end-stage renal failure. Nephrol Dial Transplant 2004; 19: 1009. [CrossRef]
18. Sjölander A, Nyrén O, Bellocco R, Evans M. Comparing different strategies for timing of dialysis initiation through inverse probability weighting. Am J Epidemiol 2011; 174: 1204-10. [CrossRef]
19. Korevaar JC, Jansen MA, Dekker FW, Jager KJ, Boeschoten EW, Krediet RT, et al. When to initiate dialysis: effect of proposed US guidelines on survival. Lancet (London, England) 2001; 358: 1046-50. [CrossRef]
20. Tang SC, Ho YW, Tang AW, Cheng YY, Chiu FH, Lo WK, et al. Delaying initiation of dialysis till symptomatic uraemia--is it too late? Nephrol Dial Transplant 2007; 22: 1926-32. [CrossRef]
21. Coronel F, Cigarrán S, Herrero JA. Early initiation of peritoneal dialysis in diabetic patients. Scand J Urol Nephrol 2009; 43: 148-53. [CrossRef]
22. Crews DC, Scialla JJ, Liu J, Guo H, Bandeen-Roche K, Ephraim PL, et al. Predialysis health, dialysis timing, and outcomes among older United States adults. J Am Soc Nephrol 2014; 25: 370-9. [CrossRef]
23. Cooper BA, Branley P, Bulfone L, Collins JF, Craig JC, Fraenkel MB, et al. A randomized, controlled trial of early versus Llate initiation of dialysis. N Engl J Med 2010;363(7):609-619. [CrossRef]
24. Access: http://www.tuik.gov.tr/PreHaberBultenleri.do?id=24644
25. Süleymanlar G, Ateş K, Seyahi N. Registry 2016 T.C. Sağlık Bakanlığı ve Türk Nefroloji Derneği Kayıt Sistemi Ortak Raporu: Türk Nefroloji Derneği Yayınları, 2017;10.
26. Esposito C, Torreggiani M, Arazzi M, Serpieri N, Scaramuzzi ML, Manini A, et al. Loss of renal function in the elderly Italians: a physiologic or pathologic process? J Gerontol A Biol Sci Med Sci 2012; 67: 1387-93. [CrossRef]
27. Obi Y, Kimura T, Nagasawa Y, Yamamoto R, Yasuda K, Sasaki K, et al. Impact of age and overt proteinuria on outcomes of stage 3 to 5 chronic kidney disease in a referred cohort. Clin J Am Soc Nephrol 2010; 5: 1558-65. [CrossRef]
28. Murtagh FEM, Marsh JE, Donohoe P, Ekbal NJ, Sheerin NS, Harris FE. Dialysis or not? A comparative survival study of patients over 75 years with chronic kidney disease stage 5. Nephrol Dial Transplant 2007; 22: 1955-62. [CrossRef]
29. Wong CF, McCarthy M, Howse MLP, Williams PS. Factors affecting survival in advanced chronic kidney disease patients who choose not to receive dialysis. Ren Fail 2007; 29: 653-9. [CrossRef]
30. Smith C, Da Silva-Gane M, Chandna S, Warwicker P, Greenwood R, Farrington K. Choosing not to dialyse: evaluation of planned non-dialytic management in a cohort of patients with end-stage renal failure. Nephron Clin Pract 2003; 95: c40-6. [CrossRef]
31. Carson RC, Juszczak M, Davenport A, Burns A. Is maximum conservative management an equivalent treatment option to dialysis for elderly patients with significant comorbid disease? Clin J Am Soc Nephrol 2009; 4: 1611-9. [CrossRef]
32. Hussain JA, Mooney A, Russon L. Comparison of survival analysis and palliative care involvement in patients aged over 70 years choosing conservative management or renal replacement therapy in advanced chronic kidney disease. Palliat Med 2013; 27: 829-39. [CrossRef]
33. Da Silva-Gane M, Wellsted D, Greenshields H, Norton S, Chandna SM, Farrington K. Quality of life and survival in patients with advanced kidney failure managed conservatively or by dialysis. Clin J Am Soc Nephrol 2012; 7: 2002-9. [CrossRef]

34. O'Connor NR, Kumar P. Conservative management of end-stage renal disease without dialysis: A systematic review. J Palliat Med 2012; 15: 228-35. [CrossRef]
35. Jager KJ, Ocak G, Drechsler C, Caskey FJ, Evans M, Postorino M, et al. The EQUAL study: A European study in chronic kidney disease stage 4 patients. Nephrol Dial Transplant 2012; 27 Suppl 3: iii27-31. [CrossRef]
36. van de Luijtgaarden MW, Noordzij M, Tomson C, Couchoud C, Cancarini G, Ansell D, et al. Factors influencing the decision to start renal replacement therapy: results of a survey among European Nephrologists. Am J Kidney Dis 2012; 60: 940-8. [CrossRef]
37. Streja E, Nicholas SB, Norris KC. Controversies in timing of dialysis initiation and the role of race and demographics. Semin Dial 2013; 26: 658-66. [CrossRef]
38. Slinin Y, Guo H, Li S, Liu J, Morgan B, Ensrud K, et al. Provider and care characteristics associated with timing of dialysis initiation. Clin J Am Soc Nephrol 2014; 9: 310-7. [CrossRef]