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Original Article

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What Has Changed with the Implementation of National Cadaveric Kidney Allocation Policy in Turkey?

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ABSTRACT

Objective: Previously, transplant centers in Turkey were free in selecting a potential recipient from their own local waiting list of deceased donor renal transplantation, and commonly patients with lower risk were selected. In May 2008, the Turkish Health Ministry issued a national cadaveric kidney allocation policy based on a pointing system. This system increased the equity but might have decreased the utility by elevating the risk of complications with possibly worse graft and patient survivals. We aimed to determine the short and medium-term effects of the new system on graft and patient survival.
Methods: Forty-seven cadaveric renal transplant recipients who were transplanted before this system and 80 cadaveric renal transplant recipients who were transplanted under the new system were included. Short and medium-term transplant-related parameters were compared between the groups.
Results: Patients transplanted after 2008 were older, had longer cold ischemia time, higher rates of delayed graft function, and early acute rejection. However, medium-term glomerular filtration rate, graft, and patient survivals were not different between patients transplanted before and after 2008.
Conclusion: The new system in Turkey increased the opportunity for transplantation of previously disadvantageous patients and did not have a significant negative effect on medium-term renal functions.
Keywords: Graft survival, kidney allocation, mortality

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INTRODUCTION

Renal transplantation is the best treatment for end-stage kidney disease and provides better survival and higher quality of life compared to hemodialysis and peritoneal dialysis.[1-3] Transplantation from cadaveric donors constitutes about 25% of all kidney transplants in Turkey.[4] Ideally, cadaveric kidney allocation policies shall maintain a perfect balance between equity and utility. Before May 2008, organ transplant centers in Turkey were free in selecting the recipient candidate from their own local waiting lists for transplantation in the case of a cadaveric kidney donation provided the blood group is matched. Centers possibly considered young and low-risk patients who had no or minimal comorbid diseases and had not undergone a previous transplant in order to get better results. This approach may have resulted in a low chance of transplantation for older patients with higher dialysis duration and several comorbidities and also for broadly sensitized patients with a history of previous transplantations.

In May 2008, the Turkish Ministry of Health issued a new national cadaveric kidney allocation policy. According to this new system, when a graft is offered to an organ transplant center, listed potential recipients of the center get points based on age, dialysis duration, level of human leucocyte antigen (HLA) match with the donor, and proximity to the donor location. The graft must be transplanted to the patient with the highest point.[5] Obviously, this system increased the equity but probably decreased

the utility by elevating the risk of complications with possibly worse graft and patient survivals. In this single-center study, we aimed to find out the short and medium-term effects of this new system on graft and patient survival.

METHODS

The study was conducted on 127 renal transplant recipients that were transplanted from a cadaveric donor between January 1, 2001 and January 1, 2017 in transplantation unit of Haccettepe University Medical Faculty Hospital. Forty-seven of the patients had been transplanted before the change in the cadaveric kidney allocation system (May 2008), and 80 of the patients had been transplanted under the new system. Inclusion criteria were age > 18 years at the time of transplantation and a follow-up of at least 3 months after transplantation. Demographic characteristics including age, sex, etiology of chronic kidney disease, donor age and sex, HLA typing of the recipients and donors, cold ischemia time, presence of delayed graft function (DGF), episodes of acute rejections, graft losses, mortalities, and duration of post-transplantation hospitalizations were recorded from the electronic database of the hospital and from patient files. Serum creatinine, glomerular filtration rate (GFR), and 24-h proteinuria values at the time of discharge and during the follow-up period were recorded. All these parameters were compared between patients that were transplanted before and under the new allocation system. The study was approved by the local ethics committee of Hacettepe University Medical Faculty before the study began and was conducted in accordance with the Declaration of Helsinki.

Statistical Package for Social Sciences version 20 for Windows (IBM SPSS Corp.; Armonk, NY, USA) was used for statistical analysis. Continuous variables were presented as mean ± standard deviation or median (min-max), and categorical variables were presented as numbers and percentages. Chi-square test was used to determine the relationship between categorical variables. The normality of the distribution of the continuous variables was determined by the Shapiro–Wilk test; homogeneity of variances was analyzed with the Levene test. Variables with normal distribution were compared by Student *t*-test while Mann–Whitney *U* test was used for the variables with non-normal distribution. Kaplan–Meier test was used in survival analyses. $P < .05$ was considered statistically significant.

Main Points

- Demand for cadaveric kidneys far exceeds the supply.
- Cadaveric kidney allocation policies are extremely important for the optimum use of this scarce number of kidneys.
- Cadaveric kidney allocation policies should maintain a balance between efficiency and equity.
- National cadaveric kidney allocation system in Turkey increased the equity.
- National cadaveric kidney allocation system in Turkey did not have a significant negative effect on medium-term renal functions.

RESULTS

The mean age of the cadaveric renal transplant recipients was 40.0 ± 12.7 years, and 65 of 127 patients (51.2%) were male. The mean age of their donors was 31.1 ± 19.1 years while 94 of 127 donors (74.0%) were male.

The demographic and clinical characteristics of patients who were transplanted from a cadaveric donor before the change in organ allocation system (n = 47) and under the new system (n = 80) are shown in Table 1. Patients that had received cadaveric graft after the implementation of the new policy were significantly older which was also true for their donors. There were no significant differences with regard to sex distribution of recipients and donors and etiology of primary kidney disease.

Short-term clinical and laboratory parameters of patients who were transplanted from a cadaveric donor before the change in organ allocation system and after the change in the system are presented in Table 2. Patients transplanted under the new kidney allocation policy had longer cold ischemia times, higher incidence of DGF, lower GFR at the time of discharge, and higher rates of acute rejection within the first 3 months of transplantation.

Renal functions at the end of the first year of transplantation for patients that were transplanted from a cadaveric donor before the change in organ allocation system and after the change in system are shown in Table 3. There were no differences with regard to renal functions at the end of the first year in both groups.

Mean follow-up duration was 9.9 years for patients transplanted from a cadaveric donor before May 2008 and 4.6 years for patients transplanted from a cadaveric donor after this date. The number of biopsy-proven rejections were 17/47 and 28/80, respectively, in both groups. A significantly higher percentage of patients transplanted under the new system suffered acute rejection when a shorter follow-up duration was considered. Eleven (23.4%) of the patients transplanted before 2008 and 11 (13.7%) of the patients transplanted after 2008 lost their grafts. Kaplan–Meier analysis did not reveal a significant difference for graft loss between the two groups (P = .703). Three (6.4%) of the patients transplanted before 2008 and seven (8.7%) of the patients transplanted after 2008 died. Kaplan–Meier analysis did not reveal a significant difference in mortality between the two groups (P = .283).

DISCUSSION

This study revealed that the new cadaveric policy in Turkey that was established in May 2008 increased the chance of transplantation of older patients with fewer HLA matches with the donor. Although some of the short-term parameters including cold ischemia time, rates of DGF, GFR at discharge, and rates of acute rejection in the first 3 months were worse in the new system, there were no significant differences for medium-term results.

Table 1. Demographic and Clinical Characteristics of Patients That Were Transplanted from a Cadaveric Donor Before and Under the New Kidney Allocation Policy

	All Patients (*n* = 127)	Transplanted Before New Kidney Allocation Policy (*n* = 47)	Transplanted Under New Kidney Allocation Policy (*n* = 80)	*P*
Age (years)	40.0 ± 12.7	33.6 ± 10.5	43.7 ± 12.5	<.0001
Gender (*n*, %)				.984
Male	65 (51.2%)	24 (51.1%)	41 (51.2%)	
Female	62 (48.8%)	23 (48.9%)	39 (48.8%)	
Primary kidney disease (*n*, %)				.946
Urological	31 (24.4%)	11 (23.4%)	20 (25.0%)	
Glomerulonephritis	24 (18.9%)	9 (19.2%)	15 (18.7%)	
Amyloidosis	11 (8.7%)	4 (8.5%)	7 (8.8%)	
Polycystic kidney	8 (6.3%)	3 (6.4%)	5 (6.3%)	
Diabetes	3 (2.4%)	1 (2.1%)	2 (2.5%)	
Miscellaneous	13 (10.2%)	4 (8.5%)	9 (11.2%)	
Unknown	37 (29.1%)	15 (31.9%)	22 (27.5%)	
Donor age (years)	31.1 ± 19.1	25.0 ± 16.3	38.1 ± 19.9	.01
Donor Gender (*n*, %)				.726
Male	94 (74.0%)	34 (72.1%)	60 (75.0%)	
Female	33 (26.0%)	13 (27.9%)	20 (25.0%)	
Mean HLA match (*n*)	2.13 ± 1.23	2.46 ± 1.23	2.01 ± 1.23	.007

HLA, human leucocyte antigen.

The new kidney allocation system in Turkey forced the transplant centers to record their patients to a national system. In the case of a cadaveric kidney donation, candidates from the same blood group with the donor get points according to the criteria defined in Table 4.[5] In this scoring system, transplant centers are ranked according to the total score of their three patients with the highest score, and the graft kidney is directed by the Turkish Ministry of Health to the transplant center with the highest total points. This center must transplant the kidney to its patient with the highest point. If a medical barrier is detected in this patient for transplantation, lower-ranked patients are respectively evaluated.

We believe that the current kidney allocation system maintains a perfect balance between equity and utility. It aims in directing the graft to patients with better HLA match and lower cold ischemia time to increase utility, but also patients with longer waiting times will have an advantage which makes the system fair. There is also positive discrimination for pediatric patients. This system dramatically changed the graft kidney allocation in Turkey. However, there can be a theoretical concern that graft and patient survival can be significantly shortened because of transplanting higher-risk patients.

In this study, we observed an increase in the mean age of cadaveric donor transplant recipients under the new system. Points given for each month after the date patient started chronic dialysis in the new allocation system are the main reason for the increased age of recipients under the new system.

Although the mean age of cadaveric kidney donors was higher under the new system, this increase was thought to be not related to the change in allocation policy rather relaxation of donor criteria for cadaveric transplantations in recent years seemed responsible from this observation.

Not surprisingly, we observed longer cold ischemia time under the new system. This increase is mainly related to the high prevalence of panel reactive antibody (PRA) positive patients in the waiting lists and not implementing a policy based on the sensitization status of the candidates. Transplant centers receive a list of patients from the highest to lower points in the case of a cadaveric kidney donation. Patients at the top of the list are the patients with longer dialysis duration hence longer waiting times, and they are commonly PRA-positive. PRA positivity frequently results in positive cross matches and delay in surgery. Another factor is the high burden of comorbidities whose preoperative evaluation prolongs the time to surgery in these patients.

Several short-term parameters including rates of DGF, GFR at discharge, and rates of acute rejection in the first 3 months were

Table 2. Short-Term Clinical and Laboratory Characteristics of Patients That Were Transplanted From a Cadaveric Donor Before and Under the New Kidney Allocation Policy

	Transplanted Before New Kidney Allocation Policy (*n* = 47)	Transplanted Under New Kidney Allocation Policy (*n* = 80)	*P*
Cold ischemia duration (hours)	9.7 ± 4.9	15.7 ± 5.4	<.001
DGF (*n*, %)			
No	35 (74.5%)	37 (46.2%)	.002
Yes	12 (25.5%)	43 (53.8%)	
Duration of hospitalization (days)	19.3 ± 11.9	16.5±11.7	.210
GFR at discharge (mL/min/1.73 m^2)	69.7 ± 22.4	59.2 ± 27.0	.029
Rejection in first three months (n, %)			
No	44 (93.6%)	62 (77.5%)	.018
Yes	3 (6.4%)	18 (22.5%)	
Graft loss in first 3 months (*n*, %)			
No	46 (97.9%)	72 (90.0%)	.152
Yes	1 (2.1%)	8 (10.0%)	
Mortality in first three months (*n*, %)			
No	46 (97.9%)	76 (95.0%)	.651
Yes	1 (2.1%)	4 (5.0%)	

DGF, delayed graft function; GFR, glomerular filtration rate.

Table 4. Current Criteria for Cadaveric Kidney Allocation in Turkey

Criteria	Points
Degree of HLA match	In the case of full match (2A, 2B, 2DR), graft is transported to the full match recipient without considering other criteria. In the absence of full match, 150 points for each DR match 50 points for each B match 5 points for each A match.
Geographic location	1000 points if donor and recipient are in the same geographic region.
Donor hospital	250 points for recipients listed in the same hospital with the donor hospital.
Recipient age	
≤11 years	HLA match points × 2.5
12-17 years	HLA match points × 1.5
≥18 years	HLA match points × 1
Duration of dialysis	3 points for each month

HLA, human leucocyte antigen.

worse in the new system for cadaveric kidney transplant recipients. Since there is no alternative explanation, this difference probably reflects the effect of change in allocation policy.

Increased cold ischemia time could largely explain worse short-term renal functions in the new system. It is well-known that longer cold ischemia time is associated with the risk of DGF[6-8], and DGF is a major risk factor for acute rejection.[9] Increased recipient and donor ages can be possible contributing factors in the worse early renal functions under the new system. It was previously demonstrated that elderly patients are under a higher risk for DGF[10], and increased donor age is among the risk factors for acute rejection.[11]

Increased duration of dialysis unfavorably affects post-transplant renal functions.[12] Although we did not evaluate the sensitization status of the patients, those with longer dialysis vintage also have a higher probability of sensitization which is a risk factor for poor renal function.[13]

The more complicated course after early transplantation may be expected to cause a higher duration of post-transplant hospitalization. However, we could not find a change in post-transplant hospitalization duration with the implementation of the new policy. This may be explained by the unnecessary long hospitalizations in the earlier years of transplantation. Currently, patients are discharged as soon as their health

Table 3. First Year Renal Functions of Patients That Were Transplanted from a Cadaveric Donor Before and Under the New Kidney Allocation Policy

	Transplanted Before New Kidney Allocation Policy (*n* = 47)	Transplanted Under New Kidney Allocation Policy (*n* = 80)	*P*
1-year creatinine (mg/dL)	1.33 ± 0.65	1.20 ± 0.58	.189
1-year GFR (mL/min/1.73 m^2)	63.2 22.9	65.8 ± 22.5	.547
1-year proteinuria (mg/day)	474 ± 938	280 ± 328	.547

GFR, glomerular filtration rate.

condition permits them to provide the hospitalization of other next potential recipients.

The main determinants of medium-term graft function are donor factors (living vs. cadaveric, standard criteria vs. expanded criteria), age of the recipient, native kidney disease, level of HLA match, sensitization status, time on dialysis, comorbidities, DGF, and compliance on immunosuppressive treatment.[14] Although some of these parameters were different for patients transplanted before and after the new system, we did not observe a significant difference in medium-term renal functions in cadaveric kidney transplant recipients.

The effect of change in national kidney allocation policy in Turkey had been previously addressed only in a single study. Solak et al. compared the 42 cadaveric renal transplant recipients transplanted before and 42 cadaveric renal transplant recipients transplanted within 2 years after the implementation of the new system. They observed increased recipient age and pre-transplant dialysis duration with the new system and an increased percentage of hepatitis C positive transplantations. There were no differences in 1 and 3 years graft and patient survival, donor characteristics, duration of cold ischemia time, and risk of DGF.[15] Unlike this study, we included a slightly higher number of patients, a larger control group, and most importantly, we included patients transplanted in a longer period (8years before and after the new system). This difference is probably the cause of the increased age of donors after the new system in our study. GFR at discharge and early rejection rates were not reported by Solak et al. which were significantly worse under the new system in our study.

Changing kidney allocation systems in different countries yielded similar results. For example, in the United States, the kidney allocation policy changed in 2014. Grafts with longest estimated function were directed to recipients expected to benefit the longest; grafts with shorter potential function were shared in a wider geographic distribution for recipients with high mortality if not transplanted, the definition of waiting time was changed and calculated from the start of dialysis, and priority was given for candidates with high PRA.[16] Two years after this change, the percentage of kidney transplants for recipients age 50 and older increased slightly. Highly immunized patients and those with long dialysis vintage had increased transplantation compared to the previous allocation system. However, there was an increase in the percentage of patients experiencing DGF. Moreover, patient and graft survival decreased slightly.[17] In another study, it was observed that in-hospital costs and readmissions were increased with the implementation of the new system in the United States.[18]

The main limitation of this study is being a retrospective single-center study with a low number of subjects included. A lack of data on PRA levels is another limitation.

In conclusion, the new allocation system in Turkey increased the opportunity for transplantation of previously disadvantageous patients. Although some of the short-term parameters were worse with the new system, it does not have a significant unfavorable effect on medium-term graft functions. However, completely excluding the detrimental effects of the new policy on medium and long-term renal functions requires multi-centric studies with larger sample sizes.

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REFERENCES

1. Wolfe RA, Ashby VB, Milford EL, et al. Comparison of mortality in all patients on dialysis, patients on dialysis awaiting transplantation, and recipients of a first cadaveric transplant. *N Engl J Med*. 1999;341(23):1725-1730. [CrossRef]
2. Tonelli M, Wiebe N, Knoll G, et al. Systematic review: kidney transplantation compared with dialysis in clinically relevant outcomes. *Am J Transplant*. 2011;11(10):2093-2109. [CrossRef]
3. Suthanthiran M, Strom TB. Renal transplantation. *N Engl J Med*. 1994;331(6):365-376. [CrossRef]
4. Turkish Society of Nephrology. Registry of the nephrology, dialysis and transplantation in Turkey. 2018. Available at http://www.nefroloji.org.tr/folders/file/REGISTRY_2018.pdf. Accessed May 18, 2020.
5. Turkiye Cumhuriyeti Saglik Bakanligi. Ulusal Organ ve Doku Nakli koordinasyon sistemi Yönergesi. 2008. Available at https://www.saglik.gov.tr/TR,11250/ulusal-organ-ve-doku-nakli-koordinasyon-sistemi-yonergesi.html. Accessed May 18, 2020.
6. Debout A, Foucher Y, Trébern-Launay K, et al. Each additional hour of cold ischemia time significantly increases the risk of graft failure and mortality following renal transplantation. *Kidney Int*. 2015;87(2):343-349. [CrossRef]
7. Pérez Valdivia MA, Gentil MA, Toro M, et al. Impact of cold ischemia time on initial graft function and survival rates in renal transplants From deceased donors performed in Andalusia. *Transplant Proc*. 2011;43(6):2174-2176. [CrossRef]
8. Helanterä I, Ibrahim HN, Lempinen M, Finne P. Donor age, cold ischemia time, and delayed graft function. *Clin J Am Soc Nephrol*. 2020;15(6):813-821. [CrossRef] [Epub ahead of print].

9. Wu WK, Famure O, Li Y, Kim SJ. Delayed graft function and the risk of acute rejection in the modern era of kidney transplantation. *Kidney Int*. 2015;88(4):851-858. [CrossRef]
10. Gavela Martínez E, Pallardó Mateu LM, Sancho Calabuig A, et al. Delayed graft function After renal transplantation: an unresolved problem. *Transplant Proc*. 2011;43(6):2171-2173. [CrossRef]
11. Tullius SG, Tran H, Guleria I, et al. The combination of donor and recipient age is critical in determining host immunoresponsiveness and renal transplant outcome. *Ann Surg*. 2010;252(4):662-674. [CrossRef]
12. Meier-Kriesche HU, Port FK, Ojo AO, et al. Effect of waiting time on renal transplant outcome. *Kidney Int*. 2000;58(3):1311-1317. [CrossRef]
13. Lee KW, Kim SJ, Lee DS, et al. Effect of panel-reactive antibody positivity on graft rejection before or after kidney transplantation. *Transplant Proc*. 2004;36(7):2009-2010. [CrossRef]
14. Legendre C, Canaud G, Martinez F. Factors influencing long-term outcome After kidney transplantation. *Transpl Int*. 2014;27(1):19-27. [CrossRef]
15. Solak I, Sezer TO, Toz H, et al. What kind of changes occurred in clinical characteristics of deceased kidney donor recipients after national allocation system in Turkey? A single-center retrospective analysis. *Transplant Proc*. 2012;44(6):1598-1600. [CrossRef]
16. Organ Procurement and Transplantation Network. Organ Procurement and Transplantation Network. (OPTN) policies. 2016. Available at https://optn.transplant.hrsa.gov/media/1200/optn_policies.pdf. Accessed May 18, 2020.
17. United Network for Organ Sharing. The Kidney Allocation System (KAS) the first two years. 2017. Available at https://unos.org/wpcontent/uploads/unos/KAS_First-two years_041917.pdf. Accessed May 18, 2020.
18. Melanson TA, Hockenberry JM, Plantinga L, et al. New kidney allocation system associated With increased rates of transplants Among black and Hispanic patients. *Health Aff (Millwood)*. 2017;36(6):1078-1085. [CrossRef]