Evaluation of Living Kidney Donor and Recipient Candidates: The Experience of Our Center

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ABSTRACT

Purpose. We evaluated potential kidney living donors and recipients for donation in our transplant center.

Materials and methods. Candidates to be kidney living donors and kidney transplant recipients (KTxR) were retrospectively evaluated. All candidates were informed and assessed by transplant coordinator and nephrologists. All data were obtained from archive records.

Results. The mean ages of 194 kidney living donors and 182 KTxR were 45.7 ± 13.1 and 37.7 ± 14.6 years, respectively. Percentages of female candidates were 55.2% and 34.1% among kidney living donors and KTxR respectively. The kidney living donor candidates were the patients' mothers (27.3%), spouses (24.2%), siblings (21.6%), fathers (12.4%), and sons or daughters (6.2%) of KTxRs and others (8.2%). The numbers of donors with body mass index (BMI) > 30 kg/m^2 and > 35kg/m^2 were 56 (28.9%) and 17 (8.8%) respectively. Due to withdrawal from donation (21.2%) and renal problems (15.3%), 85/194 (43.8%) kidney living donors were excluded. Of the remaining 51/182 (28%) KTxR candidates, 26/182 (14.2%) were unsuitable because their panel-reactive antibody (PRA) $> 20\%$. Sixty-six KTxR were performed in our center. Nine donor candidates were rejected due to obesity (BMI > 35 kg/m^2).

Conclusion. Most of our kidney living donors were mothers, housewives, and uneducated persons. Due to high percentages of suitability among candidates of KTxRs and kidney living donors as 72% and 56% may be an advantage for living kidney donation. However, PRA positivity in the recipients drew attention as a major barrier. The high incidence of obesity among the donor candidates suggests that societies must be more sensitive about this issue.

A KIDNEY transplant is the best treatment for end-stage renal disease (ESRD) patients and is associated with a higher rate of survival, better quality of life, and less dependence on healthcare resources compared to dialysis treatment [1].

According to the United State Renal Data system, waiting time for a transplant and comorbid disease burdens in chronic dialysis patients waiting for transplant continues to increase, primarily because of the insufficient number of donor organs. While the growth rate of ESRD population has increased, the availability ratio of transplant organs has not kept up. In the last 10 years the number of adults waiting for a kidney transplant in the United States has almost doubled. There are 103,233 people waiting for a kidney transplant in the United States as of November 27, 2018 [2]. The average wait time for an individual for a first

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kidney transplant is 3.6 years, which varies based on the health status, suitability, and availability of organs [3]. In 2014, 17,107 kidney transplantations were performed in the United States, 11,570 of which were from donors and 5537 of which were from living donors [2]. Transplant centers thus use various strategies, including expanding medical admission criteria, to increase organ availability.

Although kidney transplantation is the gold standard treatment in ESRD patients, post-transplant complications affecting both donors and recipients and long-term risks are still principal problems of transplantation that need to be dealt with.

Developments in immunopharmacology have led to improvements in the management of renal transplant patients and decreases in mortality rates [4,5]. At the same time, in post-transplantation monitoring, cardiovascular diseases, infections, and malignancies have been observed to be among the significant reasons for mortality in renal transplant patients [6].

On the other hand, for a successful kidney transplant, various factors such as the level of HLA compatibility between the donor and the recipient, pre-transplant blood transfusions, the recipient's immunoreactivity, and sensitization, as well as the postoperative immunosuppressive treatment method used, are crucial [7].

Kidney transplant recipient candidates must be evaluated with care to diagnose and treat diseases that may affect post-transplantation survival. Donor selection is a critical factor for the long-term success of kidney graft, and perioperative complications related to donor nephrectomy, long-term risks such as gestational hypertension and preeclampsia in female donors, gout, hypertension, and chronic kidney failure are possible [8–11]. Up-to-date guidelines utilized in kidney transplant donor and recipient selection are important in minimalizing post-transplant complications that may develop in donors and recipients [8].

The aim of our study was to determine the reasons for the acceptance and rejection of the recipient and kidney living donor candidates for possible kidney transplantation. It was approved by the Medicine Ethics Committee of Çukurova University Faculty in March 2018 (board decision number 75/26).

MATERIALS AND METHODS

In our study, 194 living donor candidates and 182 recipient candidates for kidney transplantation at our transplant center between 2014 and 2018 were evaluated retrospectively. All the demographic, clinical, and laboratory data of the participants were obtained from the record system data created at our transplant center. All potential donor candidates were briefed about living kidney transplant and its possible risks by a transplant coordinator during their initial application to our center. Similarly, all the recipient candidates were informed about the operation, surgical, infectious and metabolic complications that could occur during the postoperative period, and immunosuppressive drugs and their side effects.

During the initial evaluation, the demographic information of every potential donor and recipient (including sex, age, height, weight, body-mass index, the biological relationship between the donor and the recipient, work, and education level) was recorded by the transplant coordinator. A general physical examination was performed by the nephrologist. Biochemical tests (including complete blood count, fasting glucose, blood urea nitrogen, serum levels of creatinine, uric acid, total protein, aspartate transaminase, alanine transaminase, sodium, potassium, calcium, phosphorus, urine examination, daily urine protein, thyroid stimulating hormone (TSH), erythrocyte sedimentation rate, and markers of viral hepatitis) were measured. An abdominal ultrasonogram and chest radiographic examination were done. Opinions of other clinics were solicited via consultation when required.

During the initial evaluation, the donor and recipient candidates suitable for living kidney transplant were hospitalized and histocompatibility antigens, cross-matching tests for recipient candidates, panel-reactive antibody (PRA) tests, and, if required, further evaluations were performed. The cross-matching test for potential recipients was performed using the complement-dependent cytotoxicity (CDC) method, while the PRA scan and description were carried out with the Luminex method. Following the evaluations, the reasons for rejection were explained in detail to the donor and recipient candidates determined to be unsuitable. Absolute contraindications for living donor kidney transplants at our center were blood pressure uncontrolled with more than one drug ($>140/90$ mm Hg), major cardiovascular disease, diabetes mellitus, human immunodeficiency virus infection, active hepatitis B and C infection, kidney stone disease, bleeding disorder, mental retardation, psychiatric disease that is active or not under control, malignancy, body mass index (BMI) >35 kg/m^2, age <21 years, glomerular filtration rate (GFR) <80 mL/min, proteinuria >300 mg/day, and kidney-related hematuria. Absolute contraindications for recipient candidates were major cardiovascular disease, malignancy, human immunodeficiency virus infection, active hepatitis B or C infection, and active infection. Kidney transplantations involving ABO incompatible patients or those with PRA $>20\%$ are not performed at our center. Following the evaluations, kidney transplantations were performed with the donor and recipient candidates determined to be suitable at our center.

STATISTICAL ANALYSIS

The data were analyzed using the SPSS 19.0 program (IBM, Armonk, NY, United States). Categorical measurements were taken using numbers and percentages, numerical measurements were taken using averages and standard deviations (and medians and minimum-maximums when appropriate). The Kolmogorov-Smirnov test was used to determine whether the quantitative measurements featured a normal distribution, the Student's *t*-test was used between independent groups when the hypothesis was fulfilled, and the Mann-Whitney U test was used when the hypothesis was not confirmed.

RESULTS

Total 194 potential living kidney donors (107 women; 55.2%) with a mean age of 45.7 ± 13.1 were admitted to our transplant center between 2014 and 2018 (Table 1). The candidates reported that they wanted to donate their kidneys to 182 recipient candidates (120 male; 65.9% male) with a mean age of 37.7 ± 14.6. One hundred and seventy-two donor candidates applied for 172 recipient

Table 1. Demographic and Clinical Characteristics of Potential Kidney Donor Candidates (N = 194)

Parameters	% (n) or Mean ± SD	Parameters (Normal Value)	% (n) or Mean ± SD
Age (y)	45.7 ± 13.05	Glucose, mg/dL (70–100)	92.4 ± 14.4
Sex (female)	55.2 (107)	Creatinine, mg/dL (.4–1)	.70 ± .171
BMI (kg/m^2)	27.9 ± 4.9	GFR, mL/min (70–120)	108.4 ± 16.05
BMI > 30, 35 (kg/m^2)	28.9 (56)/8.8 (17)	Hemoglobin, g/dL (12–16)	13.6 ± 1.99
Smoke/alcohol (yes)	28.4 (55)/2.1 (4)	WBC (4.8–10.8)	7.835 ± 2.123
HTN (previous/new)	4.6 (9)/0 (0)	ALT, U/L (7–35)	20.1 ± 10.9
DM (previous/new)	0 (0)/.5 (1)	HbA1C, % (4.8–6)	5.52 ± .48
SBP, mm Hg	113.8 ± 14.7	HBsAg positive	2.6 (5)
DBP, mm Hg	71.6 ± 10.4	Anti-HCV positive	1 (2)
Blood group A, B, O, AB, %	34.5, 18.6, 44.3, 2.6		

Abbreviations: ALT, alanine transaminase; BMI, body mass index; DBP, diastolic blood pressure; DM, diabetes mellitus; GFR, glomerular filtration rate; HCV, hepatitis C virus; HTN, hypertension (blood pressure > 140/90); SBP, systolic blood pressure; SD, standard deviation; WBC, white blood cell.

candidates, 16 donor candidates applied for 8 recipient candidates, and 6 donor candidates applied for 2 recipient candidates. Kinship relationships of donors to recipient candidates were as follows: mother (53, 27.3%); spouse (47, 24.2%); sibling (42, 21.6%); father (24, 12.4%); son or daughter (12, 6.2%); and other (16, 8.2%). According to their educational levels, the donor candidates comprised illiterate (66, 34%), literate (10, 5.2%), primary school (69, 35.6%), secondary school (19, 9.8%), high school (21, 10.8%), and university (9, 4.6%). Donor candidates' professions included housewife (92, 47.4%), laborer (32, 16.5%), unemployed (11, 5.7%), officer (5, 2.6%), tradesman (1, 0.5%), and others (36, 18.6%). Eighty-five (43.8%) donor candidates were found unsuitable as a result of the evaluations; the reasons why are presented in Table 2. Renal reasons for donors being rejected were proteinuria (3), hematuria (2), nephrolithiasis (2), kidney cyst (2), low GFR (3), and renal mass (1). Of the recipient candidates, 119 (65.4%) were undergoing hemodialysis and 8 (4.4%) were undergoing peritoneal dialysis, while 51 (28%) were preemptive and 4 (2.2%) were stage V kidney transplant patients. Of the 182 recipient candidates, 51 (28%) were found to be unsuitable to be a recipient (Table 2). The most frequent reason for unsuitability was a PRA > 20%. At our center 66 kidney transplantation were performed; 66 out of 194 (34%) donors and 66 out of 182 (36.2%) recipient candidates were approved.

DISCUSSION

Our transplant center is part of a university hospital and provides transplant services free of charge to those with health insurance. In the last 4 years, 109 (56.2%) out of 194 donors and 131 (71.9%) out of 182 recipient candidates who applied to our transplant center were determined to be suitable for a kidney transplantation. Transplantations were performed for 60.5% of the recipients determined to be suitable based on the evaluations with suitable donors (50.3%) at our center. In a study, 37% of the candidates were determined to be suitable for a kidney transplant in a study carried on 146 donor candidates within a 4-year monitoring period [12]. Similar to our findings, another study found that 52% of 133 donor candidates were suitable for a kidney transplant within a 5-year period [13].

Of the kidney transplantations performed at our center, 34% (66/194) involve living donors. In another study, transplantations were performed for 139 donor candidates over 7 years, at about the same rate as our study [14].

The reasons our donor candidates are rejected for kidney transplantation are as follows, in order of frequency: withdrawal from consideration; renal problems; blood group incompatibility; and incomplete tests. The main objective of donor evaluation is to ensure that the donor candidate is healthy, has normal kidney function and structure, does not have any infectious diseases that can be transmitted to the recipient, and will not encounter unacceptable risks after

Table 2. Causes of Rejection of Potential Kidney Donors (n = 85) and Recipients (n = 51)

Problem	Donor % (n)	Problem	Recipient % (n)
Withdrawal	21.2 (18)	PRA > 20%	51 (26)
Renal	15.3 (13)	PRA > 20%, female/male	27.5 (14)/23.5 (12)
Hematologic	14.1 (12)	GFR (> 20 mL/dk)	15.7 (8)
Incomplete Study	14.1 (12)	Surgical	9.8 (5)
Chronic Hepatitis	7.1 (6)	Cardiac	7.8 (4)
Obesity	10.6 (9)	Incomplete study	5.9 (3)
Pulmonary	3.5 (3)	Incompatible cross-match	2 (1)
Other	12.9 (11)	Pulmonary	2 (1)
		Gastrointestinal	2 (1)
		Obesity	2 (1)
		Ethics committee decision expected	2 (1)

Abbreviation: PRA, panel reactive antibody.

donation. Judging by the fact that the volunteer rate among our donor candidates was 96.9%, withdrawal from donation may be related to their increased concern over the donation or their choice of other centers for transplant.

Renal problems (15.3%) leading to the rejection of our potential donor candidates included proteinuria, low GFR, hematuria, nephrolithiasis, kidney cyst, and renal mass. The Kidney Disease Improving Global Outcomes (KDIGO) donor evaluation guidelines suggest that an acceptable kidney function level is a GFR of 90 mL/min per 1.73 m^2 or greater for kidney donation. They also suggest that approval of donor candidates with a GFR of 60–89 mL/min per 1.73 m^2 should be decided on a case-by-case basis, but those with a GFR less than 60 mL/min per 1.73 m^2 should not donate [8]. Our donors with GFR 46 mL/min per 1.73 m^2 were rejected. Three of our donor candidates were rejected due to proteinuria. In previous guidelines, < 150 mg/day proteinuria was the acceptable threshold for donor candidates [15]. In a meta-analysis in which 4793 living donor candidates were examined within the scope of 42 studies and a monitoring period of 7 years on average, while there was significant heterogeneity among the studies, the proteinuria frequency was 20% in some studies and $< 5\%$ in others [16]. The KDIGO 2017 guidelines recommend that donor candidates with urine albumin excretion greater than 100 mg/day should not donate [8].

Two of our donor candidates were rejected due to persistent microscopic hematuria. One also had proteinuria < 500 mg/day, and in the other donor, asymmetric GFR accompanying hematuria was detected. In a study evaluating 512 donor candidates, persistent microscopic hematuria (14, 2.7%) was reported to manifest as thin basement membrane disease (5 cases) and IgA nephropathy (1 case) [17]. Persistent microscopic hematuria may be related to urologic anomalies (stone, tumor, etc) or glomerular diseases. Donor candidates with hematuria from a reversible cause (eg, treated infection) are suggested as being suitable for donation [8]. In our study, 2 (2.2%) out of 136 donors were rejected for kidney stones diagnosed by abdominal ultrasonography. The asymptomatic renal stone rate in 377 living donor candidates (diagnosed using abdominal computed tomography) was reported to be 5% [18]. An assessment of stone recurrence risk should be carried out prior to accepting a donor candidate with previous or current kidney stones, and a suitable decision should be made based on the possible risk of developing kidney stones after donation.

The third most common reason for rejecting donor candidates was blood group incompatibility (14.1%). In the United States, blood group incompatibility between potential living donors and recipients is over 35% [19]. Blood group incompatibility is a significant barrier for living donor kidney transplantation. The increase in organ problems in recent years has led to the development of various strategies to overcome the barrier of ABO antibodies. Desensitization protocols are provided with apheresis or B cell depletion, accompanied by strong immunosuppression. Therefore, the risk of developing infectious complications has increased [20]. The failure of 12 of our donor candidates to complete their testing may be related to the fact that the donor candidates' tests were not performed due to problems with recipient candidates, or their deciding later to apply to other centers.

Among our potential donor candidates, the frequencies of BMI > 30 kg/m^2 and BMI > 35 kg/m^2 were 28.9% and 8.8%, respectively. The frequency of obesity (BMI > 35 kg/m^2) among our rejected donor candidates was 10.6% (9/85). It is known that obese patients are subject to a high rate of perioperative complications, including wound and surgical site infections [21]. Obesity may also be a risk factor for several kidney diseases, especially obesity-related glomerulopathy [22]. In evaluating living kidney donor candidates in previous guidelines, a BMI > 35 kg/m^2 was regarded as an absolute or relative contraindication [15,23]. The KDIGO 2017 guidelines suggest that the decision to approve donor candidates with BMI > 30 kg/m^2 should be made on a case-by-case basis, taking medical conditions and demographic factors into account [8].

Of our recipient candidates, 71.9% (131/182) were accepted for kidney transplantation. The most common reason for being deemed ineligible for kidney transplantation was PRA positivity. Pre-transplant HLA sensitization due to blood transfusion, pregnancy, etc, are other major barriers to organ transplant [24].

Four patients (2.1%) had chronic allograft nephropathy stage 5T chronic kidney disease. We were not able to calculate the blood transfusion numbers. As is widely known, PRA positivity is the leading cause of low success levels of organ transplant and graft survival. The presence of these antibodies is related to antibody-mediated rejection and early graft loss [25–27]. The PRA levels of 169 of our potential recipient candidates were examined. Among the recipient candidates, the positivity levels of PRA class 1 and PRA class 2 were found to be 26 (15.4%) and 30 (17.8%), respectively. In their study, Lopes et al reported the positivity levels of PRA class 1 and PRA class 2 to be 10% and 5.2%, respectively, in 269 non-sensitized recipient candidates [24]. In another study involving 560 recipient candidates, the positivity levels of PRA class 1 and PRA class 2 were detected to be 8.7% and 15%, respectively [28]. In our center, we prefer kidney transplantation for patients with PRA $< 20\%$. Nevertheless, there are centers performing successful organ transplants with desensitization protocols in Turkey.

The majority of our kidney donors are mothers, spouses, and siblings. Turkey's organ donation laws allow up to fourth-degree relatives to be living donors for an organ transplantation. It has been found that as the level of education rises, the number of donor candidates decreases. Surprisingly, university graduates represented a small percentage of the potential donors; most of the other candidates listed their profession as either housewife or laborer.

The limitations of our study include its retrospective structure, acquisition of data from recipient and donor files, the single-center structure of the study, and the relatively

inefficient donor number. In consequence of our evaluations, the most significant causes for our candidates to be rejected were determined to be withdrawal from the donation, renal problems, blood group incompatibility in donors, and PRA positivity in recipient candidates. It was interesting that donor obesity was a barrier to transplantation as well being a danger in and of itself.

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