Revista de nefrología, diálisis y transplante
ISSN: 0326-3428
ISSN: 2346-8548
ban@renal.org.ar
Asociación Regional de Diálisis y Trasplantes Renales de Capital Federal y Provincia de Buenos Aires
Argentina

Simsek, Arife; Doğan, Sait Murat; Gurbuz, Huseyin; Ulutas, Ozkan; Toplu, Sibel; Turgut, Aslı; Yildirim, Ismail Okan; Bayindir, Yasar; Taskapan, Hulya; Sahin, Idris; Unal, Bulent; Piskin, Turgut

Living donor kidney transplantation: Why potential donors and recipients do not achieve it. Malatya Algorithm

Revista de nefrología, diálisis y transplante, vol. 40, no. 4, 2020, October-, pp. 304-310
Asociación Regional de Diálisis y Trasplantes Renales de Capital Federal y Provincia de Buenos Aires
Argentina

Rev Nefrol Dial Traspl. 2020;40(4):304-10

Living Donor kidney Transplantation: Why Potential Donors and Recipients do not Achieve it. Malatya Algorithm

Por qué los Donantes Vivos y los Receptores Potenciales no Proceden al Trasplante de Riñón, Algoritmo de Malatya

Arife Simsek[1], Sait Murat Doğan[1], Huseyin Gurbuz[2], Ozkan Ulutas[3], Sibel Toplu[4], Aslı Turgut[3], Ismail Okan Yildirim[5], Yasar Bayindir[4], Hulya Taskapan[3], Idris Sahin[3], Bulent Unal[1], Turgut Piskin[1]

ABSTRACT

Introduction: In some countries, organ donation is not widespread enough due to medical, cultural, ethical and socioeconomic factors. Living-donor kidney transplant constitutes the main source of kidney donation. Aim: To evaluate the causes of cancellation of living-donor kidney transplant and improve the effectiveness of transplant programs. **Methods:** Medical records of possible donors and recipients who were evaluated for living-donor kidney transplant at a tertiary medical center between November 2010 and September 2019 were reviewed retrospectively. **Results:** Evaluations were performed on 364 potential donors and 338 living-donor kidney transplant recipients; 207 of the latter (61.24%) underwent living-donor kidney transplant. Immune disorders represented the majority of cancellations (38.84%). Fifty-six donors (15.38%) were rejected mainly due to renal disorders (39%). **Conclusion:** Timely referral of patients to transplant centers must be guaranteed in order to overcome immune problems. Transplant centers should invest in programs adequate both for their resources and for their patients: paired kidney exchange, desensitization protocols, future research, etc.

Keywords: kidney transplant; living kidney donor

RESUMEN

Introducción: En algunos países la donación de órganos no es suficiente debido a factores médicos, culturales, éticos y socioeconómicos. El donante vivo de riñón constituye la principal fuente de donación de riñones. **Objetivo:** Evaluar las causas de cancelación de los donantes vivos de riñón y mejorar la eficacia de los programas de trasplante. **Material y métodos:** Se evaluaron retrospectivamente los registros médicos de posibles donantes y receptores para trasplante de riñón con donante vivo en un centro terciario, entre noviembre de 2010 y septiembre de 2019. **Resultados:** Se evaluaron 364 donantes potenciales y 338 receptores de trasplante de riñón con donante vivo; 207 receptores (61,24%) se sometieron a trasplante de riñón con donante vivo. Los problemas inmunológicos ocasionaron la mayoría de las cancelaciones (38,84%). A cincuenta y seis donantes (15,38%) se les negó la donación, principalmente debido a problemas renales (39%). **Conclusión:** La derivación oportuna de los pacientes a los centros de trasplante debe garantizarse para superar las barreras inmunológicas. Los centros de trasplante deberían invertir en programas adecuados, tanto por sus recursos como por los pacientes: protocolos de desensibilización, trasplante renal cruzado, investigación futura, etc.

1) Inonu University, School of Medicine, Department of General Surgery, Malatya, Turquía
2) Inonu University, School of Medicine, Department of Transplant Coordinator of General Surgery, Malatya, Turquía
3) Inonu University, School of Medicine, Division of Nephrology, Malatya, Turquía
4) Inonu University, School of Medicine, Department of İnfectious Diseases, Malatya, Turquía
5) Inonu University, School of Medicine, Department of Radiology, Malatya, Turquía

Correspondencia:
Dr. Arife Simsek
ORCID: 0000-0002-4807-3597
draksimsek@yahoo.com.tr

Financiamiento:
Ninguno.

Conflicto de intereses:
Ninguno que declarar.

Recibido: 8-03-2020
Corregido: 12-04-2020
Aceptación: 23-04-2020

ISSN 0326-3428

Palabras Clave: trasplante renal; donante de riñón vivo

INTRODUCTION

Kidney transplantation is the best treatment for end-stage renal disease (ESRD).[1] Ninety thousand-three hundred and six kidney transplants were performed worldwide in 2017, 63.5% of them were from deceased donors.[2] Although living donations, especially in a preemptive settings, have excellent outcomes, the proportion of living kidney donor transplantations (LKDT) has continued to fall. Despite its benefits, LKDT is the least common treatment option in the United States and does not exceed 2.5% of all transplantations in Poland.[3-4] Live kidney donors (LKDs) may face short and long term complications, such as death, kidney complications requiring intervention, and an increased risk of cardiovascular and renal diseases.[3, 5-7] The proportion of kidney complications including readmission, re-operation, vascular complications, and other complications requiring intervention at 6 weeks, 6 months, and 1 year were 5.4%, 7.4% and 8.9%, respectively.[3] In some countries, the level of organ donation is not sufficient due to medical, cultural, ethical and socioeconomic factors, and LKDs constitute the main source of donor kidneys. LKDs are the only source of organ donor pools in 13 countries (Armenia, Ethiopia, Georgia, Honduras, Jordan, Iceland, Kenya, Mongolia, Nigeria, North Macedonia, Pakistan, Sudan and Syria).[2]

Living kidney donor transplantations accounted for most transplant procedures at our center. This article considers the Malatya Algorithm in the selection of potential donors and recipients for LKDTs and aims to improve the efficacy of transplant programs by evaluating the causes of cancellations in LKDTs.

MATERIAL AND METHODS

Patients and evaluation process

Medical records (stored in the database of our transplant center "Transplantation Dialysis and Monitoring System") of potential donors and recipients, who were evaluated for LKDT at a tertiary center between November 2010 and September 2019, were retrospectively reviewed. The donors were limited to recipients within a fourth degree of consanguinity; otherwise, approval was obtained from the Ethics Committee of the Health Ministry.

At our transplant center, evaluation of LKDs was conducted according to the principles set out by the Amsterdam Forum.[8] A six-step process (the Malatya Algorithm) was used for evaluation of both potential kidney donors and recipients. **(Table 1)**

Table 1. The six-step evaluation (Malatya Algorithm) for live donor kidney transplantation

The Evaluation Steps	Performed by
Step 1 Clinical evaluation	
All patients with ESRD requiring RRTs are informed about RRTs and superiority of renal transplantation along with complications that may arise in both recipients and living donors	Nephrology/PN outpatient clinic
If patients want to progress in renal transplantation, even if LKDT, they are registered on the waiting list	Transplant coordinator
The potential recipients are informed about ABO compatible donors (confirmed by laboratory results) within a fourth degree of consanguinity (otherwise, approval shall be obtained from the ethics committee of the Health Minister). The ABO incompatible pairs were informed about the paired-kidney exchange program, which we performed, and the medical procedure to overcome the ABO antibody barrier if they would like to choose other transplant centers. Informed consent was obtained from both potential donor and recipients to go on evaluation processes.	Nephrology/PN outpatient clinic Transplant coordinator
After psychiatric evaluation, complete medical history and physical examination of both potential donor and recipients (including comprehensive oral & dental examination) are carried out, and pairs with obvious conditions that contraindicate the transplantation (presented in **Table 2**) are excluded.	Psychiatry outpatient clinic Nephrology/PN outpatient clinic

The Evaluation Steps	Performed by
Step 2 Laboratory evaluation	
Hematology tests - Blood group was confirmed one more time - Immunologic tests - Complete blood count, routine biochemical tests, coagulation profile, serology tests (hepatitis A, B, C, HIV, CMV, EBV, HSV, Toxoplasma, Rubella, Syphilis, Brucella, Tuberculosis), thyroid function tests, PTH (routine for recipients) PSA (if needed), pregnancy test (if needed), glucose tolerance test (if needed). **Urinary tests and assessment of renal function** - Complete urinalysis, measurement of protein excretion rate & GFR **Stool tests** - Fecal occult blood test **Microbiological tests** - Urine culture, fecal culture, nasopharyngeal culture	Nephrology/PN inpatient service Immunology department
Step 3 Pre-anesthetic cardiovascular and pulmonary evaluation & Clinical consultation	
Chest x-ray, electrocardiogram, echocardiography (routine for recipients), stress test (if indicated), coronary artery angiography (if indicated), pulmonary function tests (if indicated) Basic oncologic check-up procedures & collaboration with healthcare staff in other disciplines when needed	Nephrology/PN inpatient service Other disciplines
Step 4 Urinary system evaluation	
Abdominal sonography Renal magnetic resonance imaging (if needed) Computed tomography angiography for LKDs Renal scintigraphy for LKDs (if needed) Voiding cystourethrography (if needed), Cystoscopy and ureteroscopy (if needed), Biopsy (if needed)	Urology Radiology Nuclear medicine Transplantation surgery Nephrology/PN inpatient service
Step 5 Decision making in LKDT	Multidisciplinary committee
Step 6 Scheduling patients' surgeries	Transplantation surgery

The obvious conditions of both potential donors and recipients that contraindicated transplantation were eliminated in the initial stage **(Table 2)**.

Early exclusion procedures were carried out by the nephrologists. Following early exclusion, the evaluation process was conducted by a multidisciplinary committee (transplant surgeons, nephrologists/pediatric nephrologists (PNs), urologists, immunologists, infectious diseases specialists, anesthesiologists, radiologists, cardiologists, obstetricians and gynecologists, and the transplant coordinator). ABO incompatible kidney transplantations were not performed in our center because they were not covered by the requisite medical insurance. The ABO incompatible pairs were informed about the paired-kidney exchange program, which we performed, and the medical procedures to overcome the ABO antibody barrier if they wished to choose other transplant centers.

Age, gender, previous history, the relationship between the pairs, and reasons for cancellation were recorded for both potential donors and recipients. The following recipient characteristics were also recorded: underlying renal disease, duration of chronic renal disease (CRD), preemptive/dialysis phase, dialysis type, time on dialysis, previous history of kidney transplantation, whether LKDT was performed afterward, and mortality.

 ISSN 0326-3428

Table 2. The obvious conditions of both potential donors and recipients that contraindicate the transplantation

Potential Donors	Potential Recipients
Age < 18 years	
BMI > 35 ABO incompatible (confirmed by laboratory results)	
Refusing participation in evaluation process	Refusing participation in evaluation process
Presence of substance abuse, psychosocial instability	Presence of substance abuse, psychosocial instability
Having medical problems (complicated diabetes, uncontrolled hypertension, renal diseases, severe cardiovascular/pulmonary diseases, active infection, or malignant diseases)	Having medical problems (severe cardiovascular or pulmonary diseases that may complicate the anesthetic management, active infection, or malignant diseases)

Statistical analysis

Data were analyzed using SPSS 17.0 for Windows. Descriptive frequencies were obtained for the demographic characteristics of the potential donors and recipients. The data were reported as mean ± standard deviation for normally distributed variables.

Ethics Committee Approval

The study was conducted according to the principles set out by the Helsinki Declaration of 1975. Approval from the Ethics Committee of the Institution was obtained.

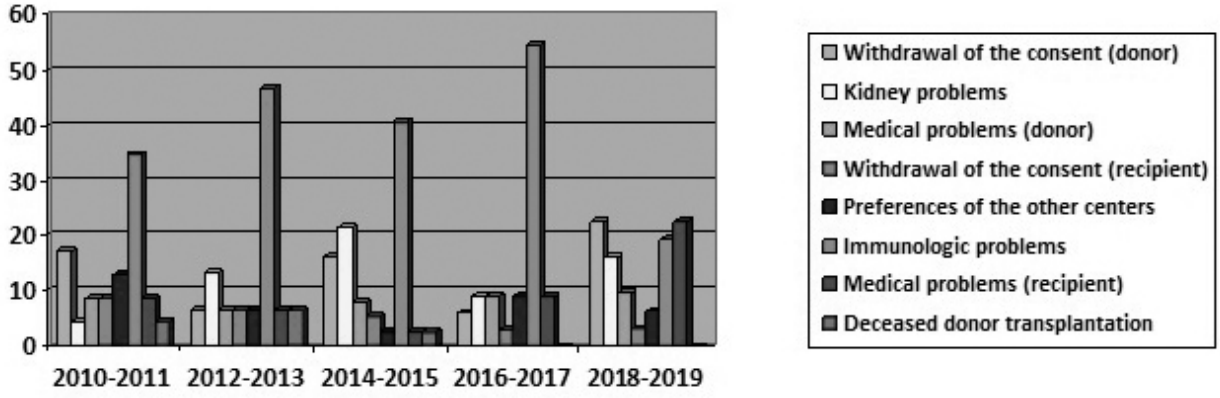
RESULTS

Two hundred and eighty-seven kidney transplantations were performed between November 2010 and September 2019. LKDTs accounted for 72.1% of the procedures. A total of 364 potential donors and 338 recipients were evaluated for LKDT. One potential donor applied for 314 recipients, 2 potential donors applied for 22 recipients, and 3 potential donors applied for 2 recipients. Of the 338 recipients, 207 (61.24%) underwent LKDT. **Table 3** presents the reasons for LKDT cancellation. Most of the reasons (58.2%) were recipient-related, immunologically incompatible pairs constituted 38.84% of all cancellations. Immunological problems have dropped below 20% in the last 2 years **(Figure 1)**. Among medical problems, which interfered with transplantation, 7 recipients had malignant diseases, 4 had active infections, 2 had complicated cardiovascular diseases and one had active ulcerative colitis.

Table 3. The causes of cancellation in living donor kidney transplantation

The causes		N (%)
Donor related	The withdrawal of the consent	20 (14.3)
	Kidney problems (anatomical and functional)	19 (13.6)
	Medical problems	12 (8.6)
Recipient related	The withdrawal of the consent	7 (5.03)
	The preferences of the other centers	10 (7.19)
	Immunologic problems	50 (35.9)
	Medical problems	14 (10.07)
Donor & recipient related	Immunologic problems and Kidney problems	3 (2.15)
	Immunologic problems and High body mass index	1 (0.71)
Deceased donor kidney transplantation		3 (2.15)
TOTAL		**139 (100)**

Figure 1. The causes of cancellation in live donor kidney transplantation over the last ten years



Among 364 potential donors, 55 (15.10%) were rejected for kidney donation, of whom 24 (43.6%) were men and 31 (56.3%) were women. The mean age was 48.78 (range: 24-75) years. Of the 55 donors, 22 (40%) had kidney problems, while 20 (36.3%) refused to proceed to donation. Twelve donors had medical problems such as complicated cardiovascular and pulmonary diseases (n=5), complicated diabetes mellitus (n=3), infectious (n=1) and malignant diseases (n=2) and ankylosing spondylitis (n=1). One donor had a high body mass index.

Of 131 recipients, who did not proceed to LKDT, 77 were on dialysis (62 on hemodialysis, 15 on peritoneal dialysis). Forty-four recipients (33.5%) underwent LKDT afterward, 17 (38.6%) of them were performed at our center. Most of those transplantations (75%) proceeded with different donors **(Table 4)**. Eighteen patients (21.4%; 18/84) died while on the transplant waiting list, five deaths occurred during the evaluation process.

Table 4. The characteristics of 44 recipients who underwent LDKT afterward

Causes of cancellation	**Total (%)**	**At different center (61.3%)**		**At our center (38.6%)**	
		Same donor (N)	**Different donor (N)**	**Same donor (N)**	**Different donor (N)**
The preferences of the other centers	22.7	10	-	-	-
The withdrawal of the consent (donor)	20.4	-	6	-	3
The withdrawal of the consent (recipient)	2.2	-	-	-	1
İmmunologic	20.4	1	7	-	1
Kidney problems in donor	18	0	3	-	5
Medical problems in donor	13.6	-	-	-	6
Medical problems in recipient	2.2	-	-	1	-

DISCUSSION

There were 538 potential recipients on the waiting list of our center. Like national data, in which LKDs are the main source of organs (78.47%),[9] LKDTs accounted for 72% of the 287 transplantations performed between November 2010 and September 2019. Among patients, who were evaluated for LKDTs, 21.4% died while awaiting an organ. Given the fact that mortality is higher among patients who have no LKDs, the development of novel strategies must be encouraged to increase the availability of

 ISSN 0326-3428

donor organs.

The selection of recipients for LKDTs is a standard process and does not differ among centers. However, relative contraindications for LKDs vary among centers. Donor evaluation is essential not only to eliminate the risk of complications for the donors, but also to increase the survival of both graft and recipient. At our center, evaluation of LKDs was conducted according to the principles set out by the Amsterdam Forum and 308 of 364 potential donors (84.6%) were approved for donation.

Most of the disqualifications were recipient-related (58.2%), immunologically incompatible pairs constituted a significant percentage (38.84%) of the cancellations. Although desensitization protocols have been used in accordance with current knowledge, immunological problems have only dropped below 20% in the last 2 years. To overcome immunologic barriers the public should be informed about the superiority of preemptive transplantation. Timely referral of patients to the transplant centers by the nephrologist and/or dialysis center specialists may reduce immunologic risk by preventing unnecessary blood transfusions. The paired-kidney exchange program (center-based, national-based, and international-based, like those in Europe)[10] should be adopted and implemented. Future research should also be supported.

The deceased donor kidney transplantation (DDKT) was the promising cause for LKDT cancellations (2.15%). The kidney problems of potential donors (15.7%) and the medical problems of both potential donors and recipients (18.7%) were not preventable reasons for LKDT cancellation and were not diagnosed at the initial stage because complex and invasive tests were carried out only after simple and essential investigations had confirmed transplant suitability.

The pairs' refusal of LKDT and/or preferences for other centers may increase the economic burden on the healthcare system. Each center proceeds with its own evaluation of both recipients and donors independent of any previous evaluation process. In the current study, 10 potential recipients preferred to go to other centers, 20 potential donors and 7 recipients did not want to proceed to the evaluation stage, this decision by 37 pairs (26.6% of all cancellations) therefore resulted in unnecessary increases in health expenditures. In addition to driving up healthcare costs, those pairs increased the workload of the transplant team. It was not determined why 20 potential donors and 7 recipients did not wish to proceed to evaluation and why 10 potential recipients preferred treatment at other centers. The pairs, especially the potential donors, must give informed consent completely voluntarily. No pressure should ever be brought to bear to persuade the pairs to become participants in LKDT. They should be adequately informed about LKDTs and the performance of the transplant center through a variety of modalities. Our transplant center adheres strictly to these rules. The Government/Social Health Insurance covers organ transplantations for both donor and recipient. This is thought to significantly reduce the potential economic burden that the pairs would otherwise incur and may account for their preferring other centers.

In conclusion, to reduce educational barriers to organ donation, several strategies should be employed, including public and professional meetings. In cases of organ shortage, all barriers to LKDT should be removed as far as is possible to encourage pairs to participate in available programs. Timely referral of patients to the transplant centers by the nephrologist and/or dialysis center specialists must be ensured. Transplant centers should invest in programs suitable for their resources and patients, such as paired-kidney exchange (center-based, national-based, and international-based), desensitization protocols, future research etc.

BIBLIOGRAPHY

1) Schena FP. Epidemiology of end-stage renal disease: international comparisons of renal replacement therapy. *Kidney Int*. 2000;57(Suppl. 74):S39-S45. doi: 10.1046/j.1523-1755.2000.07407.x
2) Global Observatory on Donation and Transplantation. International report on organ donation and transplantation activities, executive summary 2017 [Internet]. Disponible en: <http://www.transplant-observatory.org/> (consulta: 25/03/2020).
3) OPTN/UNOS (Organ Procurement and Transplantation Network)/United Network for Organ Sharing) National Data Reports, Transplants by Donor Type, latest data 2017 [Internet]. Disponible

en: <https://optn.transplant.hrsa.gov/data/view-data-reports/national-data/> (consulta: 25/03/2020).

4) Ciszek M, Pączek L, Łuków P, Rowiński W. Effective optimization of living donor kidney transplantation activity ensuring adequate donor safety. *Ann Transplant*. 2012;17(3):103-10. doi: 10.12659/aot.883464.
5) Friedman AL, Peters TG, Jones KW, Boulware LE, Ratner LE. Fatal and nonfatal hemorrhagic complications of living kidney donation. *Ann Surg*. 2006;243(1):126-30. doi: 10.1097/01.sla.0000193841.43474.ec.
6) Muzaale AD, Massie AB, Wang MC, Montgomery RA, McBride MA, L Wainrigh JL, *et al*. Risk of end-stage renal disease following live kidney donation. *JAMA*. 2014;311(6):579-86. doi: 10.1001/jama.2013.285141.
7) Mjøen G, Hallan S, Hartmann A, Foss A, Midtvedt K, Øyen O, *et al*. Long-term risks for kidney donors. *Kidney Int*. 2014;86(1):162-7. doi: 10.1038/ki.2013.460.
8) Ethics Committee of the Transplantation Society. The consensus statement of the Amsterdam Forum on the Care of the Live Kidney Donor. *Transplantation*. 2004;78(4):491-2. doi: 10.1097/01.tp.0000136654.85459.1e.
9) Turkish Transplantation Foundation. [Statistics, 2002-2018 Turkey tables and graphs related to organ donation and transplantation] [Internet]. Disponible en: <http://www.tonv.org.tr/tr/organ-bagisi/istatistikler> (consulta: 25/03/2020).
10) Council of Europe Reference Documents; European Directorate for the Quality of Medicines. Kidney Exchange Programmes in Europe Position Paper of the Council of Europe European Committee on Organ Transplantation (CD-P-TO). *Newsletter Transplant*. 2018;23(1):76-80.

 ISSN 0326-3428