Exclusion Reasons of Living Kidney Donor Candidates: A Single-Center Experience

Canlı Böbrek Nakli Verici Adaylarının Elenme Nedenleri: Tek Merkez Deneyimi

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ABSTRACT

OBJECTIVE: Due to severe organ shortage, living kidney donors are important choices for transplantation. In Muslim countries, such as Turkey, living kidney donors are the main source of donor pool. In the literature, reasons for living donor exclusion are reported from several countries. However, there is no published study that focused on exclusion reasons of donor candidates in Turkey where living kidney transplantation rate is 73.4%. The goal of this retrospective study was to examine the exclusion reasons for donation among living kidney donor candidates at a single center in Turkey.

MATERIAL and METHODS: A total 538 adults were evaluated as a living kidney donor candidate between December 1988 and January 2012. Evaluation outcome, exclusion reasons and demographic data were examined from electronic file system and immunology laboratory records.

RESULTS: In this period 451 kidney transplantations (38.6% cadaveric, 61.4% living donor) was performed. Overall 261 (48.5%) donor candidates who underwent evaluation could not donate. We were able to find the precise cause of exclusion of 86 donors (33%). Among excluded donor candidates the most common exclusion reason was medical causes (64%) such as diabetes mellitus, low glomerular filtration rate and hypertension.

CONCLUSION: Our study suggests that medical causes are significant exclusion reasons for living kidney donation at our center.

KEY WORDS: Kidney transplantation, Living kidney donor, Donor evaluation, Exclusion reason

ÖZ

AMAÇ: Organ bağışının istenilen düzeyde olmaması nedeni ile canlı böbrek nakli verici adayları, böbrek nakli için önemli kaynak oluşturmaktadır. Türkiye gibi Müslüman ülkelerde bu durum daha da belirgindir. Literatürde çeşitli ülkelerden böbrek nakli için canlı verici adaylarının elenme nedenlerini bildiren çalışmalar mevcuttur. Canlı böbrek nakli oranının %73,4 olduğu ülkemizden ise verici adaylarının elenme nedenlerine yönelik bir çalışma bulunmamaktadır. Çalışmamızın amacı, retrospektif olarak canlı böbrek nakli verici adaylarının elenme nedenlerini değerlendirmektir.

GEREÇ ve YÖNTEMLER: Çalışmaya Aralık 1988 ve Ocak 2012 tarihleri arasında merkezimize böbrek nakli verici adayı olarak başvurmuş 538 kişi dahil edilmiştir. Elektronik dosyaların ve immünoloji laboratuvar kayıtlarının taranması ile adaylık değerlendirme sonuçları, elenme nedenleri ve demografik bilgileri değerlendirilmiştir.

BULGULAR: Çalışma süresince merkezimizde 451 böbrek nakli (%38,6 kadaverik, %61,4 canlı) gerçekleştirilmiştir. Adaylardan 261 (%48,5) kişi verici olamamıştır. Seksen altı (%33) adayın kesin elenme nedenine ulaşabilmiştir. Diyabetes mellitus, düşük glomerüler filtrasyon hızı ve hipertansiyon gibi medikal nedenler en önemli (%64) elenme nedeni olarak belirlenmiştir.

SONUÇ: Merkezimize başvuran canlı böbrek nakli verici adaylarının, en sık elenme nedeni medikal nedenler olarak tespit edilmiştir.

ANAHTAR SÖZCÜKLER: Böbrek nakli, Canlı böbrek vericisi, Verici değerlendirmesi, Elenme nedeni

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INTRODUCTION

Kidney transplantation (KTx) is one of the treatment choices for individuals with end-stage renal failure. Severe deceased donor organ shortage and long waiting times on the deceased donor list remains a worldwide serious problem. Living kidney donors are becoming more important source for transplantation because of organ shortage. Also different religions have some striking aspects on organ donation and transplantation (1). Many individuals within the faith are still reluctant, particularly regarding deceased donation. Therefore, most transplants in many predominantly Muslim countries are still live donations. The yearly average of living kidney transplantation (LKTx) in USA is 37.9% in the past 5 years (2).Deceased donor KTxin Iran comprises about 13% of the whole annual experience, while the numbers are 25 to 30% in Turkey, Saudi Arabia and Kuwait (3).At the end of 2011, LKTx is %73.4 of all KTx patients in Turkey (4).The Department of Religious Affairs has declared that "organ donation after death or from living subjects is appropriate in Turkey" (with decision number 396/13 dated March 3, 1980). Islam has no restriction against transplantation thats why it would be wrong to associate the low deceased kidney transplantation rate with religion only. The impression of religious concerns or other factors on donation isn't the main purpose of our study so we would not discuss these issues here.

Evaluation and exclusion reasons of living donor candidates might differ among centers, although there are some international consensus reports on the standard definition for the evaluation of living donor candidates (5-8). Obesity, hypertension, low estimated glomerular filtration rate (GFR) are the major contraindications for donor exclusion in the literature of several countries (9-13). There is no published study that focused on exclusion reasons of living kidney donor (LKD) candidates in Turkey. This retrospective study aimed to examine the reasons for exclusion of LKD candidates evaluated at a single center in Turkey.

PATIENTS and METHODS

Study Population

We performed a retrospective study involving LKD candidates who underwent first time evaluation at the University of Uludag Transplantation Center between December 1988 and January 2012. Data were collected by review of electronic patient files and immunology laboratory records. Evaluation outcome, exclusion reasons and demographic data were examined.

Living Donor Candidate Evaluation

Potential transplant recipients are informed about LKTx at our center. We first interview with recipient and potential LKD candidate as a team which consists of nephrologist and transplant coordinator. Interested LKD candidates are asked several questions to evaluate absolute or relative contraindications for donation. Absolute contraindications are <18 years old, chronic illness (heart, lung and liver, autoimmune or neurologic disease), proteinuria and/or hematuria, impaired renal function (GFR <80 mL/min/1.73 m^2), complicated diabetes mellitus (DM) or hypertension, urologic abnormalities of donor kidney, chronic active viral infection, active malignancy, malignancy or melanoma histories, uncontrolled psychiatric disorder, active drug abuse, coagulation disorders, pregnancy, nephrocalcinosis, bilateral or recurrent kidney stones. Relative contraindications are active peptic ulcer disease, renovascular disease (multiple renal arteries etc.), obesity (BMI >35kg/m^2), kidney stone, hypertension or DM family histories, controlled hypertension or Type 2 DM.

Candidates without contraindications have initial ABO blood typing, tissue typing and lymphocyte cross-match performed. For HLA Typing, peripheral blood was collected by venipuncture in vacuum tubes containing EDTA anticoagulant, and genomic DNA was extracted using EZ-DNA reagent, according to the manufacturer's instructions. One Lambda LABType® SSO kit was used in combination with the Luminex™ technology (XMap 200; Luminex, Austin, TX) for typing of HLA class I (HLA-A and -B) and class II (HLA-DRB1) alleles.

Cellular crossmatching was performed on total lymphocytes separated from peripheral blood. For CDC crossmatching, 2 μL serum+1 μL cells (2×106/mL) were incubated for 60 min at room temperature with and without DTT. Five microliters complement (rabbit serum) was added and incubated for 60 min at room temperature. Cytotoxicity was visualized using acridine orange/ethidium bromide cocktail and evaluated by using inverted fluorescence microscope.

We do not perform both ABO-incompatible and HLA-incompatible renal transplantations at our center. Cross-match compatible donor candidates undergo routine laboratory tests. If no clear contraindications to donation identified, further evaluation and radiologic tests are performed. Donor candidates may be excluded at the initial meeting or during the evaluation. The final decision is made by our transplantation team that consisting of nephrologist, urologist, immunologist, anesthetist, radiologist and transplant coordinators.

Before 2008, all kidney donations were done by open live-donor nephrectomy with standard dorsal lumbotomy. Since then, laparoscopic living donor nephrectomy has been performed at our center.

The numerical and categorical variables were expressed as the mean ± standard deviation and ratios, respectively.

RESULTS

At our center 451 kidney transplantations were performed between December 1988 and January 2012, and 277 (61.4%) of 451 were living kidney transplantation. Among living donors, 90.9% is from living related (mother 41.1%, father 32.7%, sister-brother 13.5%, child 1.5% and other related 2.5%), and 9.1% is from living unrelated (spouse 8% and other 0.7%) donor (Table I).

A total 538 candidates was evaluated for LKD. Two hundred seventy seven (51.5%) donors successfully donated at our center. Two hundred sixty one candidates (48.5%) could not donate. The mean age of these donor candidates was 52.4±10.9 years (range 24-72). One hundred fifty (57.4%) donor candidates were female. Among 261 donor candidates, recipients of 21 LKD candidates (8%) had cadaveric transplantation, and recipients of 26 LKD candidates (10%) had LKTx from another donor. 13 (5%) had donated at another transplantation center, 115 (44%) were withdrawn before evaluation was completed (Table II).

The precise causes of exclusion of 86 donors (33%) were able to achieve. In excluded donors the reasons were medical causes (n=55, 64%), HLA-incompatibility and cross-match positivity (n=23, 26.7%) and psychosocial reasons (n=8, 9.3%) (Table III).

Table I: Donor characteristics of transplantations at our center (n: 451).

		n (%)
Deceased donor		174 (38.6)
Living donor		277 (61.4)
Related		252 (90.9)
	Mother	114 (41.1)
	Father	89 (32.7)
	Sister-brother	37 (13.5)
	Child	4 (1.5)
	Other *	8 (2.5)
Unrelated		25 (9.1)
	Spouse	24 (8)
	Other	1 (0.7)

*Aunt, uncle, grandparent.

Table II: Outcomes in living kidney donors (n: 538).

	n (%)
Donated	277 (51.5)
Not-donated	261 (48.5)
Cadaveric Tx	21(8)
Tx from another donor	26 (9.9)
Tx at another center	13 (4.9)
Withdrawn	115 (44)
Excluded	86 (33)

Tx: Transplantation.

Table III: Exclusion reasons in excluded living kidney donors.

	n (%)
Medical causes	55 (64)
Histocompatibility	23 (26.7)
Psychosocial	8 (9.3)

Table IV: The medical causes in excluded living kidney donors.

Medical causes	n (%)
Diabetes mellitus	9 (16.3)
Low GFR	7 (12.7)
Hypertension	6 (10.9)
Viral hepatitis Donor Recipient	 6 (10.9) 5 (9)
Malignancy	5 (9)
Urological abnormalities	4 (7.2)
Other	7 (12.7)
Recipient died	2 (3.6)
Chronic infection of recipient	4 (7.2)

Other: Primary hyperparathyroidism, cerebrovascular accident, chronic anemia, cardiac valvular disease, colonic fistula.

Among donor candidates excluded for medical reasons, the most common diagnosis overall was DM (n=9, 16.4%), followed by inadequate creatinine clearance (n=7, 12.7%), hypertension (n=6, 10.9%), viral hepatitis (n=6, 10.9%), malignancy (n=5, 9.1%), urologic abnormalities (n=4, 7.3%), medical causes of recipient (n=11, 20%) and other medical causes (n=7, 12.7%). Other medical reasons for non-donation of potential donor candidates were primary hyperparathyroidism, cerebrovascular accident, chronic anemia, cardiac valvular diseases and colonic fistula. Chronic hepatitis C virus (HCV) and B virus (HBV) infections were the diagnosis of the donor candidates who were excluded because of viral hepatitis. Six (3 HCV, 3 HBV) donor candidates had viral hepatitis (Table IV).

Eleven potential donors could not donate because of medical problems of the recipients. Two of the recipients died during the evaluation process. Five recipients had chronic viral hepatitis (4 HCV, 1 HBV) and 4 had other chronic infections.

Of the 23 excluded donors 12 were excluded based on HLA mismatch and 11 were excluded based on positive cross-match results. The significant psychosocial reason was only unwillingness of donation.

DISCUSSION

Access to organs for transplantation has varied among countries because of differences in communities. Religion is one of the major determinants for an organ donation (1). Living kidney donors are main source for transplantation especially in Muslim countries, including Turkey; under the influence of social structure and lack of education. We could not evaluate religious and sociocultural factors in this retrospective study. However, faith was not a possible cause of donation refusal in most of these candidates as they were admitted to our transplant center for organ donation.

The evaluation for potential living donor varies among transplant centers as well as countries. There are international consensus reports on the standard definition for the evaluation of LKD (5-8). Medical causes such as obesity, hypertension and DM are the significant exclusion reasons for living kidney donation (9-13). Other significant exclusion reasons in our study were medical causes (64%). The distribution of the medical causes differs from the other studies, since obesity and hypertension were not prominent exclusion reasons in our study.

Most transplantation centers exclude potential donors with an impaired fasting glucose (≥126 mg/dL) or abnormal a two-hour oral glucose tolerance test (OGTT). At our center all donor candidates have fasting plasma glucose estimation, and those who have impaired fasting glucose, family history for DM or gestational diabetes undergo a two-h OGTT. In the presence of DM suspicion, we perform fundus examination and microalbuminuria screening to determine microvascular complications. Candidates with complicated DM are excluded at our center. The donor who has glucose intolerance without diabetic complications and the recipient are informed about risk that might be seen after donation. After the interview if they accept LKTx under these conditions, the candidate could donate at our center. Recently, a study from Japan suggests that candidates who have glucose intolerance without diabetic complications might donate safely (14).

Hypertension has been considered an absolute or relative contraindication for donation at different centers. At the Amsterdam Forum on the Care of the Live Kidney Donor, hypertensive donors with easily controlled hypertension who are older than 50 years, have GFR ≥80 mL/min and urinary albumin excretion <30 mg/day were accepted as kidney donors (5). Some studies reported that kidney donors might have increased blood pressure after donation (15, 16). In contrast to these studies, some others showed no adverse effects regarding blood pressure, GFR or urinary protein excretion after donation of hypertensive LKD (17-19). At our center, if the recipient had no other LKD candidate and/or has waited on the cadaveric list for too long, both recipient and donor candidate are informed about the risks that might be seen after donation. If living donation is accepted, the potential hypertensive donor undergoes further evaluation including echocardiography, fundus examination, microalbuminuria and 24–h ambulatory blood pressure monitoring to determine end-organ damage. Potential hypertensive donors whose blood pressure is controlled with more than one antihypertensive drug or with end-organ damage could not donate. Lower percentage of hypertension (10.9%) as an exclusion reason might be related to the acceptance of the low-risk hypertensive donors. We have not experienced any serious problem of transplantations from non-complicated diabetic or hypertensive donors.

Obesity is another reported significant exclusion reason (9, 20). According to UNOS guidelines grade I obesity (BMI 30-35 kg/m^2) is relative, BMI >35 kg/m^2 is absolute contraindication for living donation (21). Although obesity prevalence is high in our city (22), only 2 excluded donor candidates were obese. One of them had DM and the other one was hypertensive.

HIV, HBV or HCV infection of the donor is usually a contraindication to living donation. HCV positive donors are generally excluded before further evaluation. These candidates may only be considered for donation to a HCV positive recipient, if the donor PCR is negative (23). Hepatitis B surface antigen positive donor candidates are also excluded. The high percentage of viral hepatitis as an exclusion reason in our study might be related to the unawareness of donor candidates of their viral serology. An important part of donor candidates had their first medical tests when they were admitted as a potential donor. We detected positive viral serology at 6 potential donors. Three of them were positive for HCV and the other 3 for HBV.

HLA mismatches, cross-match positivity and ABO-incompatibility have been considered absolute contraindications to donation at some centers. ABO and/or HLA incompatible transplantation and paired donor exchange programs aim to expand the living donor pool. Despite the high hyper acute rejection risk and low graft survival rate, some centers perform ABO and/or HLA incompatible living kidney transplantation (24). Desensitization protocols and heavy immunosuppression have to be used to minimize the risks. Life-threatening infections, late onset malignancies and high cardiovascular risk are the probable complications of heavy immunosuppression. We did not perform ABO and/or HLA incompatible transplantation at our center in this study period.

Although LKDs are the main source of the donor pool in our country, awareness of the transplant protocol is not satisfactory. After the interview with candidate or the investigations, he/she might change his/her mind. Unwillingness is not significant among our candidates due to the strong family bounds. Among all living donors in 2011 in our country, 68% were from living related (mother 25.9%, father 15.3%, sister-brother 16.1%, child 2.6% and other related 8.2%), and 31.8% were from living unrelated (spouse 26.4% and other 5.4%) (3), in accordance with our results. According to an analysis of the OPTN/UNOS registry, the number of unrelated living donors has also increased

dramatically over the past decade, accounting for 28% of all living donor transplants in 2010, and being the major source of LKD kidney transplants since 2008 (2).

To expand the donor pool as a reason of extended donor criteria, old donors are used more commonly. Definition of an old donor might differ but donors over 60-65 years are considered old donors (25). Graft and recipient survival were reported to be lower when the donor was over 60 years (26). An observational study showed no significant difference of graft survival between old and young donors (27). Old donor transplantation provides better results than deceased donor transplantation (25). Advanced age is not considered a contraindication for donors at our center. We decide on the donation of old donors based on the same criteria as young donors. Also old donors with GFR below 80 mL/min/1.73 m^2 are excluded. GFR of old donors is expected to be lower as a result of GFR loss with aging. Inadequate creatinine clearance was an important medical exclusion reason in our study. At our center, 73.8% of LKD were parents of the recipients who were mostly elderly. Advanced age of the potential donors might be a reason of low GFR.

There are several limitations of our study. First of all, since this is a single-center retrospective study, larger multicenter studies are needed to evaluate LKD candidate exclusion reasons especially in countries where LKDs are the main source of the donor pool. Secondly, the data were obtained from electronic files and records and there were many missing data. Some important data like detailed medical history of potential donors was not available. Finally, the number of withdrawn candidates is also high. Nevertheless this is the first study focused on exclusion reasons of living donation in Turkey.

In conclusion, living kidney transplantation is the main type of transplantation in our country. Although the exclusion percentage (48.5%) is high, 61.4%of all transplantation is from LKD since December 1988 at our center. Medical reasons are the major impediments to living kidney donation at our center in Turkey as well. Potential LKDs have medical conditions that may be associated with their own future health risk, as well as long-term allograft dysfunction. However, there are remarkable variations in many aspects of LKD evaluation in Turkey. Variability includes acceptance criteria regarding age, DM, hypertension and BMI. More prospective studies focused on long-term results of transplantations from LKD with these relative contraindications are still needed.

REFERENCES

1. Oliver M, Woywodt A, Ahmed A, Saif I: Organ donation, transplantation and religion. Nephrol Dial Transplant 2011; 26: 437-444
2. Freitas MC: Kidney transplantation in the US: An analysis of the OPTN/UNOS registry. Clin Transpl 2011: 1-16
3. Einollahi B: Cadaveric kidney transplantation in Iran: Behind the Middle Eastern countries? Iran J Kidney Dis 2008; 2: 55-56
4. Kidney Transplantation. In: Suleymanlar G, Altiparmak MR, Seyahi N, Trabulus S (eds), Registry of the Nephrology, Dialysis and Transplantation: Registry 2011. İstanbul: Pasifik Reklam ve Tanıtım, 2012; 28-35
5. Delmonico F: A Report of the Amsterdam Forum On the Care of the Live Kidney Donor: Data and medical guidelines. Transplantation 2005; 79: S53-66
6. Pham PC, Wilkinson AH, Pham PT: Evaluation of the potential living kidney donor. Am J Kidney Dis 2007; 50: 1043-1051
7. Sachdeva M, Bhaskaran M, Molmenti EP, Dalton D, Mattana J: Approach to the pretransplant evaluation of the living kidney donor. J Transplant 2011; 2011: 245738
8. Kher A, Mandelbrot DA: The living kidney donor evaluation: Focus on renal issues. Clin J Am Soc Nephrol 2012; 7: 366-371
9. Lapasia JB, Kong SY, Busque S, Scandling JD, Chertow GM, Tan JC: Living donor evaluation and exclusion: The Stanford experience. Clin Transplant 2011; 25: 697-704
10. Zhao WY, Zhang L, Han S, Zhu YH, Wang LM, Zhou MS, Zeng L: Evaluation of living related kidney donors in China: Policies and practices in a transplant center. Clin Transplant 2010; 24: E158-162
11. Gabolde M, Herve C, Moulin AM: Evaluation, selection, and follow-up of live kidney donors: A review of current practice in French renal transplant centres. Nephrol Dial Transplant 2001; 16: 2048-2052
12. Norman SP, Song PX, Hu Y, Ojo AO: Transition from donor candidates to live kidney donors: The impact of race and undiagnosed medical disease states. Clin Transplant 2011; 25: 136-145
13. Hidalgo G, Tejani C, Clayton R, Clayton R, Clements P, Distant D, Vyas S, Baqi N, Singh A: Factors limiting the rate of living-related kidney donation to children in an inner city setting. Pediatr Transplant 2001; 5: 419-424
14. Okamoto M, Suzuki T, Fujiki M, Nobori S, Ushigome H, Sakamoto S, Yoshimura N: The consequences for live kidney donors with preexisting glucose intolerance without diabetic complication: Analysis at a single Japanese center. Transplantation 2010; 89: 1391-1395
15. Guvence N, Oskay K, Ayli D: The assessment of long-term clinic and laboratory data of living related kidney donors. Transplant Proc 2012; 44: 1614-1617
16. Boudville N, Prasad GV, Knoll G, Muirhead N, Thiessen-Philbrook H, Yang RC, Rosas-Arellano MP, Housawi A, Garg AX: Meta-analysis: Risk for hypertension in living kidney donors. Ann Intern Med 2006; 145: 185-196
17. Textor SC, Taler SJ, Driscoll N, Larson TS, Gloor J, Griffin M, Cosio F, Schwab T, Prieto M, Nyberg S, Ishitani M, Stegall M: Blood pressure and renal function after kidney donation from hypertensive living donors. Transplantation 2004; 78: 276-282
18. Tent H, Sanders JS, Rook M, Hofker HS, Ploeg RJ, Navis G, Van der Heide JJ: Effects of preexistent hypertension on blood pressure and residual renal function after donor nephrectomy. Transplantation 2012; 93: 412-417

19. Santos L, Macario F, Alves R, Mota A, Campos M: Risks of living donor nephrectomy. Transplant Proc 2010; 42: 1484-1486
20. Reeves-Daniel A, Adams PL, Daniel K, Assimos D, Westcott C, Alcorn SG, Rogers J, Farney AC, Stratta RJ, Hartmann EL: Impact of race and gender on live kidney donation. Clin Transplant 2009; 23: 39-46
21. UNOS: The Organ Procurement and Transplantation Network. United Network of Organ Sharing (UNOS). 2010
22. Ersoy C, Imamoglu S, Tuncel E, Erturk E, Ercan I: Comparison of the factors that influence obesity prevalence in three district municipalities of the same city with different socioeconomical status: A survey analysis in an urban Turkish population. Prev Med 2005; 40: 181-188
23. Caliskan Y, Yildiz A: Evaluation of the medically complex living kidney donor. J Transplant 2012; 2012: 450471
24. Arunachalam C, Garrues M, Biggins F, Woywodt A, Ahmed A: Assessment of living kidney donors and adherence to national live donor guidelines in the UK. Nephrol Dial Transplant 2013; 28: 1952-1960
25. Hourmant M, Lerat L, Karam G: Donation from old living donors: How safe is it? Nephrol Dial Transplant 2013; 28: 2010-2014
26. Iordanous Y, Seymour N, Young A, Johnson J, Iansavichus AV, Cuerden MS, Gill JS, Poggio E, Garg AX: Recipient outcomes for expanded criteria living kidney donors: The disconnect between current evidence and practice. Am J Transplant 2009; 9: 1558-1573
27. Young A, Kim SJ, Speechley MR, Huang A, Knoll GA, Prasad GV, Treleaven D, Diamant, M, Garg AX: Accepting kidneys from older living donors: Impact on transplant recipient outcomes. Am J Transplant 2011; 11: 743-750