Review Article Open Access

What Disease Conditions could be Considered for Potential Therapeutic Kidney Donations?

Yoshihide Ogawa*[1], Rensuke Mannami[2], Makoto Mannami[2], Mitsuo Nishi[3] and Naoki Mitsuhata[4]

[1]*Department of Urology, Tokyo-West Tokushukai Hospital, Akishima, Tokyo, Japan*
[2]*Department of Urology, Uwajima Tokushukai Hospital, Uwajima, Japan*
[3]*Department of Urology, Saint Martin's Hospital, Sakaide, Japan*
[4]*Department of Urology, Kure-Kyosai Hospital, Kure, Japan*

Abstract

We coined the term "therapeutic kidney donation" specifically in reference to donatable kidneys that have been nephrectomized due to urologic diseases and reviewed various series of reports and empirical sporadic reports. Kidneys with small renal tumors and distal ureter tumors in addition to benign kidney pathologies have historically been used for transplantation. Some ethical problems exist in cases in which therapeutic donor kidneys are used for unrelated living transplantation but not for related transplantation. Therefore, a well-organized national project, such as the OPTN policy, is awaited. Kidneys with small renal masses are an attractive source for donation, but these organs have several unsolved problems, including locally advanced stages, high histological grades, multifocality, and distant metastasis. Further clinical studies are warranted to organize and recruit proper therapeutic kidney donation for restored kidney transplantation.

Keywords: erapeutic donor kidney; Urologic disease; Restored kidney transplantation; High-risk recipient

e OPTN/UNOS Living Donor Committee, UNOS Policy Department, coined the term "therapeutic organ donor" to describe an individual who has an organ removed as a component of their treatment for a medical problem, and their removed organ is suitable for transplantation into a transplant candidate. e committee suggested that potential therapeutic donors may have conditions, such as renal cell carcinoma (with the tumor removed a er recovery and before transplantation), ureteral trauma (a transected ureter), or maple syrup urine disease (which is the most common type of domino liver donor) [1]. Many chronic kidney disease (CKD) patients on a transplant waiting list are eagerly anticipating this new OPTN policy proposal. In this manuscript, we would like to concentrate on the kidney as a therapeutic organ and propose a list of renal conditions associated with "therapeutic donatable kidneys" which include "donatable kidneys that are nephrectomized due to urologic diseases".

e shortage of donor kidneys is a serious problem in Japan, and this trend has become worse partly because altruistic donations and paired kidney exchange programs are not currently accepted in Japan, while ABO-incompatible living kidney transplantation has increased to 30%. In addition, restored kidney transplantation by "therapeutic kidney donation" was banned by the Japanese government in 2007, with the exception of transplantations conducted as part of clinical trials. is donor shortage crisis prompts dialysis-intolerant patients to seek transplantation and donor kidneys in foreign countries, leading to an increase in transplant tourism. To reverse this situation, the Tokushukai group launched two clinical trials of therapeutic kidney donation (TKD) in 2009, which are still ongoing, to transplant restored kidney allogra s in patients without appropriate donors among their family members or who have used all of the possible living donors in their family. erefore, the Tokushukai group is attempting to save "unrescuable" dialysis patients using restored kidney transplantations conducted as part of clinical trials [2,3]. ese restored kidney transplantations include living renal transplantations conducted in clinical studies between family members using restored kidneys with small renal tumors, renal stones, ureteral tumors, ureteral strictures, or renal cysts and a clinical study of living renal transplantations between third parties using restored kidneys (partial resection and renorrhaphy) with a solitary small renal tumor. erefore, in cases of living related or altruistically donated renal transplantation using therapeutic donatable kidneys, the surgical indication for a therapeutic donor nephrectomy could be elective, while in cases of living unrelated renal transplantations, the surgical indication for a therapeutic donor nephrectomy should be relatively imperative (depending on the decision of an expert urologist regarding whether to perform nephron-sparing surgery or discard the kidney, considering that renal salvage is always a primary goal for the urologist). It is necessary to determine and discuss which conditions could be clinically implicated for potential therapeutic kidney donation (elective or imperative) and transplantation into a transplant candidate. erefore, in this communication, the relevant literature on "therapeutic kidney donors" was reviewed to identify potential disease conditions and clarify their contextual clues.

e rst organ transplant in Japan occurred at Niigata University in 1956 (T. Kusunoki) when a living kidney obtained from a patient with idiopathic renal bleeding was temporarily transplanted to a patient with acute renal failure. In 1964, a living kidney was transplanted into a patient with chronic renal failure at the University of Tokyo, which was the rst full-scale transplant intended for permanent gra ing [4]. Some empirical experiences with unrelated kidney transplantation have been conducted using therapeutic kidneys that were removed due to kidney diseases, including kidney stones and hydronephrosis; however, most of these sporadic cases were semi-con dentially managed, accepted

***Corresponding author:** Yoshihide Ogawa, Department of Urology, Tokyo-West Tokushukai Hospital, 3chome-1-1 Matsubara-cho, Akishima, Tokyo, 196-0003 Japan, Tel: +81-42-500-4433; Fax: +81-42-500-6632; E-mail: yoshihide.ogawa@tokushukai.jp

Received March 31, 2016; **Accepted** July 18, 2016; **Published** July 25, 2016

Citation: Ogawa Y, Mannami R, Mannami M, Nishi M, Mitsuhata N (2016) What Disease Conditions could be Considered for Potential Therapeutic Kidney Donations? J Clin Exp Transplant 1: 106.

locally without ethical approval, or not actually reported to the general public. erefore, only a few people were aware of the data. Mannami et al. reported their clinical experiences using a new source of 42 kidneys, which included eight cases of benign pathologies, eight of small renal cancer, eight cases of ureteral cancer, six cases of aneurysms, four cases of severe nephrotic syndrome, and four cases of ureteral stenosis, that were restored to transplant into “unrescuable” dialysis patient [5]. Kidneys that were removed due to various diseases and used for renal transplantation, according to the Japanese literature, are shown in Table 1. In Australian and Spanish reports, restored kidneys with complex cysts, benign tumors, or complicated ureteric injuries were transplanted a er nephrectomy (Table 2) [6,7]. e transplantation of kidneys removed to treat small RCCs has been reported by several investigators and performed in more than 97 patients [8]. Despite di erences in the interpretation of the risk categories of tumor transmission by Nalesnik et al. [9] several guidelines for renal transplantation unanimously accept that small renal tumors pose some risk [10,11] and encourage further expansion of the living-donor pool. e renal transplantation procedure is demanding, similar to the living kidney transplantation procedure, and has the advantages of allowing su cient time for preoperative immunological screening, short ischemic time, and potential immediate renal function; the renal transplantation procedure is also similar to deceased kidney transplantation in terms of providing bene ts to unrelated high risk recipients and also expanding the donor pool. e spirit of “Reduce, Reuse, and Recycle” or9 22.8 Td[re is also simila2dottaand19Rforme0exp

Mannami et al.[5]	Eight benign pathologies (two angiomyolipoma, 1 cavernous angioma, 1 necrosis of ureter, 1 pelvic kidney, 1 retroperitoneal chronic infection, one renal abscess, one renal cyst with calcification), eight small renal cell carcinomas, eight ureteral cancers, six aneurysms, eight severe nephrotic syndrome from 4 patients and four ureteral stenoses.
Nicol et al. [6]	Small (<3 cm) incidentally detected renal lesions, consisting of clear cell carcinoma (25), papillary carcinoma (5), chromophobe carcinoma (1), oncocytoma (4), angiomyolipoma (3), and complex/multiloculated cysts (3)
Musquera et al.[7]	Incidental renal masses, including clear renal cell carcinoma (5), chromophobe type (2), and lipoma (1)
He et al. [16]	21 kidneys with small RCCs and 3 kidneys with complicated ureteric injuries

Table 2: Therapeutics donor kidneys retrieved due to urologic disease transplanted in large series.

3.0%, 5.1%, and 12.1%; grade 3 was noted in 7.1%, 9.0% and 14.0%; and metastases at diagnosis were identi ed in 3.0%, 2.6%, and 6.0% of cases in the 2, 3, and 4 cm groups, respectively [12]. Another study [13] also con rmed similar results and concluded that the aggressive potential of small RCC increases steeply beyond a tumor diameter of 3 cm, suggesting that the threshold for selecting patients for a surveillance strategy should be set well below a tumor size of 3 cm. Smaldone et al. [14] reported a systematic review and pooled analysis of small renal masses under active surveillance (18 retrospective studies comprising 880 patients and 936 SRMs) and revealed that eighteen lesions progressed to metastases with growth rates more than double (0.8 cm/year) those of non-progressors (0.3 cm/year), but these were generally late events (mean time to metastases 40.2 months) [14]. ey also discussed one reported case of a 73-year-old male with a 2.4 cm renal mass progressing to bony metastases at 5 months with no increase in tumor size [15]. In consideration of these provocative results, the increased accuracy of diagnosis of frozen section histology performed immediately a er tumor removal or biopsy may provide insight into the inherent biology of small renal tumors.

In conclusion, further studies are warranted regarding the following two points: 1) imperative therapeutic kidney donation could include selected cases of small renal cell carcinoma, renal aneurysm, complicated ureter injury, or distal ureteral tumor and 2) elective therapeutic kidney donation may include cases of benign renal tumors (AML), renal stones, renal injury, idiopathic renal bleeding, ureteric stenosis, complex renal cysts. A large-scale national project is necessary to organize transplant surgeons and urologists to work together to recruit therapeutic kidney donations for restored kidney transplantation. is will primarily rescue "dialysis-intolerant" patients who may bene t from renal transplantation. We welcome the therapeutic organ donation policy of the United States and anticipate utilizing living donors with therapeutic kidneys to provide a solution to the worldwide organ shortage problem in the future.

References

1. OPTN/UNOS Living Donor Committee (Bolton L.). OPTN/UNOS public comment proposal: Proposal to Establish and Clarify Policy Requirements for Therapeutic Organ Donation. Available at: https://optn.transplant.hrsa.gov/media/1185/0815-05_Therapeutic_Donor.pdf
2. Ogawa Y, Mitsuhata N, Nishi M, Mannami R, Mannami M (2012) One proposal to solve the organ shortage crisis in full understanding of donor-transmitted malignancies in kidney transplantation. Am J Transplant 12: 259-260.
3. Ogawa Y, Kojima K, Mannami R, Mannami M, Kitajima K, et al. (2015) Transplantation of Restored Kidneys from Unrelated Donors after Resection of Renal Cell Carcinoma: Results from 10 Patients. Transplant Proc 47(6):1711-1719.
4. Unrelated living renal transplantation (in Japanese) Available at: http://www6.plala.or.jp/brainx/reserved2.htm
5. Mannami M, Mannami R, Mitsuhata N, Nishi M, Tsutsumi Y, et al. (2008) Last resort for renal transplant recipients, 'restored kidneys' from living donors/patients. Am J Transplant 8: 811-818.
6. Nicol DL, Preston JM, Wall DR, Griffn AD, Campbell SB, et al. (2008) Kidneys from patients with small renal tumours: A novel source of kidneys for transplantation. BJU Int 102:188-192.
7. Musquera M, Pérez M, Peri L, Esforzado N, Sebastià MC, et al. (2013) Kidneys from donors with incidental renal tumors: should they be considered acceptable option for transplantation? Transplantation 95: 1129-1133.
8. Yu N, Fu S, Fu Z, Meng J, Xu Z, et al. (2014) Allotransplanting donor kidneys after resection of a small renal cancer or contralateral healthy kidneys from cadaveric donors with unilateral renal cancer: a systematic review. Clin Transplant. 28: 8-15.
9.