Follow-up Survey of Donor Candidates for Living Related Kidney Transplantation With Prostate Cancer

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ABSTRACT

Introduction. With the increasing number of elderly kidney donor candidates due to the lack of available donors, prostate cancer has sometimes been detected in these candidates during pretransplant screening examinations. There are currently no guidelines or consensus on prostate cancer screening and treatment in donors. We retrospectively evaluated the clinical course of donor candidates with prostate cancer.

Methods. Between January 2006 and December 2016, 9 donor candidates for living related kidney transplantation were incidentally diagnosed with prostate cancer at our institution. All male kidney transplant donor candidates routinely received prostate-specific antigen (PSA) testing. The patients with PSA levels $>$ 4.0 ng/mL underwent prostate biopsies. For future kidney transplantation, treatment for localized prostate cancer was prostatectomy.

Results. Seven low- or intermediate-risk patients according to the D'Amico risk classification underwent endoscopic prostatectomy, while 2 high-risk patients underwent high dose-rate brachytherapy to prioritize prostate cancer treatment. Of the 7 who underwent surgery, 3 patients ultimately became living related kidney transplantation donors for their wives. There was no recurrence of PSA elevation after treatment.

Conclusion. This study showed that donor candidates with prostate cancer could safely donate a kidney after a thorough evaluation to exclude those with high-risk prostate cancer. Transmission of prostate cancer through kidney transplantation seems unlikely and robot-assisted laparoscopic prostatectomy may be feasible for donor candidates with localized prostate cancer.

TRANSPLANTATION is an effective renal replacement therapy for end-stage renal failure. Reflecting an aging society, cases of living related kidney transplantation (LRKT) with donors aged over 65 years have been increasing [1,2]. Japan has a high rate of LRKT, and donors aged 60 years or older accounted for 297 cases (22.3% of the total) in 2016 [1]. As the number of elderly donors increases, it is important to identify the presence of malignant disease during pretransplant screening examinations. In particular, prostate cancer detection is common in older men with the widespread use of prostate-specific antigen (PSA) screening examinations. The transmission rate of cancer through transplantation varies depending on the pathological finding and stage of cancer. It is necessary to judge the portability of kidney transplantation and set a waiting period for each case; however, there is currently no guideline or consensus on prostate cancer screening and

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Table 1. Clinical Background and Treatment in Donor Candidates With Prostate Cancer

No.	Age (years)	PSA (ng/mL)	PV (mL)	Clinical stage	Biopsy positive core rate (%)	GS	D'Amico risk classification	Treatment	BCR	Follow-up period (years)
1	61	4.71	30.7	T1c	9.1	3 + 3	Low	LRP	No	6.1
2	62	7.51	14.8	T2a	18.1	4 + 3	Intermediate	LRP	No	9.6
3	67	9.4	26.2	T1c	14.3	3 + 3	Low	LRP	No	10.7
4	67	4.38	36.6	T1c	10	3 + 3	Low	LRP	No	7.3
5	68	23.47	19.3	T3a	70	4 + 4	High	HDR	No	5.7
6	70	19.78	21	T1c	50	3 + 4	Intermediate	RARP	No	1.2
7	74	4.40	25.3	T1c	10	3 + 3	Low	LRP	No	7.8
8	74	4.48	19.6	T1c	30	3 + 4	Intermediate	RARP	No	4.6
9	68	28.12	39.9	T3a	18.1	4 + 3	High	HDR	No	7.1

Abbreviations: BCR, biochemical recurrence; GS, Gleason score; HDR, high-dose-rate brachytherapy; LRP, laparoscopic radical prostatectomy; PSA, prostate-specific antigen; PV, prostate volume; RARP, robot-assisted radical prostatectomy.

treatment in donors. We retrospectively evaluated the clinical course and status of LRKT in donor candidates with prostate cancer.

PATIENTS AND METHODS

Nine living related kidney transplant donor candidates were incidentally diagnosed with prostate cancer at our institution between January 2006 and December 2016. All male kidney transplant donor candidates routinely received PSA testing. Patients with PSA levels > 4.0 ng/mL underwent digital rectal examination and transrectal ultrasonography-guided prostate biopsies. Prostate cancer was histologically diagnosed using 10 transrectal ultrasonography-guided nontargeted needle biopsies, with an additional targeted needle biopsy if there was a suspicious area in the prostate. Clinical stage was determined by digital rectal examination, multiparametric magnetic resonance imaging (MRI), abdominal-pelvic computed tomography, and bone scintigraphy. All patients underwent multiparametric MRI before prostate biopsy.

Treatment for localized prostate cancer was either laparoscopic or robot–assisted laparoscopic prostatectomy; however, in prostate cancer with clinical stage T3a or more, we recommended radiation therapy combined with hormone therapy to prioritize prostate cancer treatment. Two patients received a dose of 18 Gy for high dose-rate (HDR) brachytherapy and 45 Gy for external beam radiation therapy, in accordance with suitable radiation treatment planned by the radiologist. Neoadjuvant hormone therapy for 6 months and adjuvant hormone therapy for 6 months were given. We introduced both a luteinizing hormone-releasing hormone agonist and nonsteroidal antiandrogen for combined androgen blockade.

Biochemical recurrence (BCR) after prostatectomy was defined as postoperative serum PSA level more than 0.2 ng/mL. BCR after HDR brachytherapy was defined as post-HDR serum PSA level 2.0 ng/mL or more above the nadir level, consistent with the Phoenix definition of BCR after radiotherapy.

Patients undergoing HDR brachytherapy were excluded as LRKT donor candidates to prioritize prostate cancer treatment. We took follow-up PSA level measurements after prostatectomy. After confirming no BCR of prostate cancer more than 1 year after prostatectomy, a retroperitoneal donor nephrectomy was performed.

RESULTS

The clinical background and treatment of 9 LRKT donor candidates with prostate cancer are shown in Table 1. The median age of the patients was 68 years, and the median PSA level was 7.5 ng/mL (range, 4.3–28.1 ng/mL). The clinical stage was T1c-T2a in 7 patients (78%) and T3a in 2 patients (22%). Of these, only 1 had a Gleason score of 8 to 10. Based on the D'Amico risk stratification, 4 patients were classified as low-risk, 3 as intermediate-risk, and 2 as high-risk. Seven low- or intermediate-risk patients underwent endoscopic prostatectomy, while 2 high-risk patients underwent HDR brachytherapy combined with hormone therapy. After prostatectomy, the pathological stage was T3a in 1 patient and none had a Gleason score of 8 to 10. The resection margin was positive in only 1 patient. There was no BCR within the follow-up period.

Status of LRKT is shown in Table 2. Of 7 patients who underwent endoscopic prostatectomy, 3 ultimately became LRKT donors for their wives. One patient planned donor nephrectomy for his daughter in the future. Three patients were excluded as donor candidates to prioritize the treatment of prostate cancer. In 2 cases, LRKT was performed after the patient's wife became the donor candidate. Only one case was abandoned for no alternative donor candidates. The transplanted kidney was engrafted in all cases.

DISCUSSION

The Amsterdam Forum 2004 considered a transplant donor acceptable if any cases of cancer can be cured and the possibility of transmitting cancer can reasonably be excluded [3]. By excluding melanoma and gynecological cancer, which

Table 2. Status of Living Related Kidney Transplantation

No.	Donor nephrectomy	Change of donor candidate	Recipient	Graft survival	Pre-/postoperative donor's sCr level (mg/mL)
1	Yes	No	Wife	Yes	1.0/1.32
2	Yes	No	Wife	Yes	0.82/1.12
3	No	No			
4	No	Yes (wife)	Son	Yes	
6	Will undergo	No	Daughter		
7	Yes	No	Wife	Yes	0.8/0.89
8	No	Yes (wife)	Daughter	Yes	

Abbreviation: sCr, serum creatinine.

Table 3. Differences in Donor Risk Category Between Old and New Italian Guidelines

	Old guideline	New guideline
Standard risk	No PC	No PC Intraprostatic PC GS $\leq$ 6
Nonstandard risk	Intraprostatic PC GS $\leq$ 6 PC with any Gleason 4	Intraprostatic PC Gleason 3 + 4 Extraprostatic PC Gleason 3 + 3
Unacceptable risk	Any extraprostatic PC PC with Gleason $\geq$ 4	PC with prevalent Gleason $\geq$ 4 Extraprostatic PC 3 + 4 Metastatic PC

Abbreviations: GS, Gleason score; PC, prostate cancer.

have a known high risk of transmission, the rate of transmitting cancer from donor to recipient is estimated at 0.025% [4]. At present, patients with colorectal Dukes' A cancer 5 years after treatment, nonmelanoma skin cancer, and cervical carcinoma in situ can be considered as transplant donors if there is no cancer recurrence for more than 5 years after treatment; however, there is no definite guideline for prostate cancer due to the lack of sufficient evidence showing transmission to a transplant recipient.

The only reported case of prostate cancer transmission occurred after a deceased heart transplantation with locally advanced cancer and lymph node metastasis [5]. In 2014, Doerfler et al [6] reviewed transplantations performed with organs procured from donors with verified prostate cancer. Deceased donors with proven prostate cancer accounted for 122 organ transplant cases including 43 kidney transplants. No transmission of cancer was observed during a mean follow-up period of 16 to 53 months. A study from Italy reported 18 cases of recipients who received a graft kidney from a donor diagnosed with prostate cancer and found no transmission during 28 months of follow-up [7].

In contrast, Penn et al [8] reported that donor-derived cancer occurred in 103 of 237 recipients transplanted from 154 donors with organ cancer, with a 29% risk of possible prostate cancer transmission. In our study, all LRKT recipients were female, so the risk of transmission was lower than that in male recipients; however, even in female LRKT recipients of male kidneys, testosterone is secreted by 5% to 10% [9]. The possibility of transmitting prostate cancer through a transplanted organ cannot be completely excluded.

Considering the curability of prostate cancer in donor candidates and the risk of transmission, it is important to exclude donors who prefer treatment for cancer. The staging of prostate cancer and identification of lymph node metastasis is essential in reducing the risk of possible transmission. Partin tables show the probability of having positive lymph nodes is over 20% for stage T3 cancer with a Gleason score of over 7 if the PSA level is over 20 ng/mL [10]. Even if the PSA level is over 10 ng/mL, the risk of positive lymph nodes is over 20% for stage T2b cancer with a Gleason score of 3 + 4, and 40% for stage T2c cancer with a Gleason score of 8 to 10 [6,10]. The risk of metastasis of localized prostate cancer with Gleason score of 4 or 5 is 22% to 38% [10,11]. The risk of lymph node micrometastasis in localized, high-risk prostate cancer is around 20% according to the D'Amico and National Comprehensive Cancer Network classification, based on enlarged lymph node dissection [12–14]. The revised Italian national guidelines in 2005 recommend accepting potential candidates with prostate cancer to extend the donor pool and introduce the function of a second opinion expert [15]. Prostatic cancer donors with prevalent a Gleason pattern of 4 and/or ascertained metastases are determined to have unacceptable risk category in the new guidelines (Table 3). Donor candidates with high-risk prostate cancer should be considered as contraindicated for LRKT. In this study, 2 cases with high-risk prostate cancer prioritized treatment over LRKT donor candidacy.

To ensure curability of prostate cancer in donor candidates, the treatment method for clinically localized prostate cancer must be considered. Recent systematic reviews have reported that the risk of overall and prostate cancer-specific mortality increases for patients treated with radiotherapy instead of surgery [16,17]. Robot-assisted laparoscopic prostatectomy may reduce the rate of positive surgical margins and BCR compared to open radical prostatectomy at experienced facilities [18–20]. In a donor candidate well enough to undergo surgery and anesthesia, robotic radical prostatectomy can be reasonable; however, the way in which a graft kidney is exported from a donor who undergoes prostatectomy at the time of donor nephrectomy must be carefully considered. We usually export a graft kidney from the caudal port site by extending the incision rather than using a Pfannenstiel incision to avoid pelvic floor adhesions.

The waiting period is also an important factor for donor candidates with prostate cancer, but there is not a standard waiting period after treatment of prostate cancer in a donor candidate. In our department, the 2-year BCR-free survival rates of in patients with either low- or intermediate-risk prostate cancer after robotic radical prostatectomy are 100% and 98.6%, respectively. We set a waiting period of at least 1 year after prostatectomy based on these outcomes and to avoid mistiming of LRKT. Our study found no BCR after treatment during a 5-year follow-up period. Although the waiting period for a donor candidate after endoscopic prostatectomy remains controversial, a 1- to 2-year waiting period may be reasonable, considering a lower BCR rate, general status of an elderly donor, and rare transmission of prostate cancer from donor to recipient.

CONCLUSION

Transmission of prostate cancer through kidney transplantation seems unlikely. Based on the current literature and the present study, it is reasonable to exclude donor candidates with PSA level $\geq$ 20 ng/mL, T3 stage tumors, and a Gleason score $\geq$ 4. This study also showed that donor candidates with prostate cancer could safely donate a kidney after a thorough evaluation that excluded those with high-risk prostate cancer. Robot-assisted laparoscopic prostatectomy seems feasible for LRKT donor candidates with localized prostate cancer. The waiting period between cancer remission and kidney donation is controversial and must be individualized for each LRKT case.

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