Radical Retropubic Prostatectomy for Localized Prostate Cancer in Renal Transplant Patients

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OBJECTIVE To investigate the feasibility of radical retropubic prostatectomy (RRP) in renal transplant recipients with clinically localized prostate cancer.

METHODS A prospective protocol was established between August 2004 and November 2007. In that period, 8 patients diagnosed with localized prostate cancer were submitted to RRP, and their clinicopathologic data were reviewed.

RESULTS The mean age (± standard deviation) at surgery was 59.6 ± 6.7 years (range, 49-67 years). All patients had T1C tumors, except for 1 with a T2A tumor. The mean preoperative prostate-specific antigen value was 4.5 ± 1.8 ng/mL (range, 1.6-7.0 ng/mL). The mean interval between renal transplantation and RRP was 89.9 ± 65.1 months (range, 40-209 months). The procedure was well tolerated without major complications, and all patients were discharged on the fifth postoperative day. There was no impairment to bladder descent caused by the presence of the allograft or the ureteroneocystostomy. Urethrovesical anastomosis was easily performed in all cases in the standard manner. Blood transfusion was needed in 2 patients (1 received 2 U and another 5 U of blood). The mean operative duration was 183 ± 29.7minutes (range, 150-240 minutes), the mean estimated blood loss was 656 ± 576 mL (range, 100-2000 mL), and no deterioration of graft function was observed. All patients were followed, and the mean follow-up was 10.5 months (range, 2-30 months). Prostate-specific antigen was undetectable in all cases during this time frame.

CONCLUSIONS Radical retropubic prostatectomy in renal transplant patients is safe, effective, and can be easily performed in the same manner as described by Walsh, regardless of the presence of the allograft. The only necessary technical modification is the avoidance of ipsilateral lymphadenectomy to prevent damage to the transplanted organ. UROLOGY 72: 1362–1365, 2008. © 2008 Elsevier Inc.

At present more men aged >50 years are undergoing renal transplantation and will receive lifelong immunosuppressant therapy.[1] Evidence suggests that renal transplant patients experience an increased risk of certain malignancies, although the evidence regarding prostate cancer is contradictory.[2,3] The number of patients with prostate cancer after kidney transplantation has also increased, although it is unclear whether this observation is not a consequence of a more intense screening of the recipients. Also, the number of recipients aged >50 years and the calculated half-life of grafts for living donors have increased in recent times.[1,4] The real incidence of prostate cancer in renal transplant patients is not well defined but can vary from levels that are lower than in the general population to levels as high as 5.8%.[5–9] In addition, some investigators have found prostate cancer in 30% of immunosuppressed men submitted for transurethral resection of the prostate, considerably higher than the rate in non-transplanted men.[10] These facts have prompted renal transplant surgeons to actively screen kidney transplant patients for prostate cancer. We have also seen more debate about the ideal treatment modality for this disease because this situation has the potential to introduce unique technical and oncologic challenges to surgeons.[11,12] We present our experience using radical retropubic prostatectomy to treat localized prostate cancer in renal transplant recipients.

MATERIAL AND METHODS

To study the feasibility and necessary technical modifications of RRP in renal transplant recipients, a prospective protocol of surgical treatment for clinically localized prostate cancer was established between August 2004 and November 2007. In that period, 8 patients were found to have prostate cancer. They were screened according to digital rectal examination (DRE) and a total PSA value (chemiluminescence; Diagnostic Products, Los Angeles,

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Table 1. Preoperative and pathologic characteristics of the 8 patients and their tumors

Variable	Patient							
	1	2	3	4	5	6	7	8
Age at surgery (y)	58	51	62	61	67	62	49	67
Donor type	CD	CD	CD	CD	CD	LNR	LR	CD
Interval, Kd Tx to RRP (mon)	59	50	76	40	60	209	177	48
Preoperative PSA (ng/mL)	1.6	5.2	4.3	7.0	2.8	6.5	4.9	3.8
Bx Gleason sum	7	7	6	6	6	6	6	6
Clinical stage	T2A	T1C	T1C	T1C	T1C	T1C	T1C	T1C
Pathologic status								
RRP Gleason sum	6	6	6	6	6	6	6	6
Stage	T2CN0Mx	T2CN0Mx	T2CN0Mx	T2CN0Mx	T2CN0Mx	T2CN0Mx	T2CN0Mx	T2AN0Mx
Margin status	Negative	Negative	Negative	Focal apex	Negative	Negative	Negative	Focal unilateral surface

CD = cadaveric; LNR = living non-related; LR= living related; Kd Tx = kidney transplant; RRP = radical retropubic prostatectomy; PSA = prostate-specific antigen.

CA) with a cut-off value of 2.5 ng/mL. We use the same threshold in non-transplanted men, on the basis of evidence that it increases the rate of cancer detection at a stage when cure is possible.[13] The diagnosis was made by transrectal ultrasound–guided biopsy (12 fragments). Radionuclide bone scintigraphy and chest radiography were performed in all prostate cancer patients, regardless of PSA value and Gleason score, because the clinical behavior of these tumors in the immunosuppression setting is not well defined. Clinical and pathologic staging was assigned according to the 2002 TNM guidelines. Patients with clinically localized prostate cancer were submitted to radical retropubic prostatectomy. The operative technique and treatment outcomes are discussed.

All kidney transplants were positioned retroperitoneally through an extended inguinal incision. Vascular reconstruction was performed at the iliac external vessels. The urinary tract was reconstructed using the non-stented Gregoir technique. Immunosuppression was achieved with the triple-drug regimen of cyclosporine, azathioprine or mycophenolate mofetil, and prednisone. Patients who underwent repeat transplantation received induction therapy in a sequential immunosuppressive regimen. The details of immunosuppression therapy have been previously reported.[14,15]

Patients were submitted to radical retropubic prostatectomy as described by Walsh.[16] Pelvic lymphadenectomy was performed in all cases but only in the opposite side of the transplant kidney to avoid injury to it. After operation all patients received standard care. They were allowed to eat, and immunosuppression was resumed on the same day. Close suction drains were used and removed as soon as drainage fell to <50 mL, which usually occurred between the third and fifth postoperative day. All patients were discharged home on the fifth postoperative day with a Foley catheter in place, which was removed after 2 weeks. Follow-up consisted of physical examination (except for DRE, which was considered unnecessary) and PSA measurements every 3 months. In each evaluation, continence and potency rates were registered. No patient had any other treatment modality for prostate cancer before the surgery.

RESULTS

Eight cancers were diagnosed (6.3%). The indication for biopsy was based on PSA elevation in all but 1 patient, who presented exclusively with abnormal findings on DRE. The preoperative characteristics and pathologic data are summarized in Table 1. Radical retropubic prostatectomy was well tolerated by all patients, and no major complications were observed. The mean age (± standard deviation) at surgery was 59.6 ± 6.7 years (range, 49-67 years). The mean interval between renal transplant and RRP was 89.9 ± 65.1 months (range, 40-209 months). The mean operative duration was 183 ± 29.7 minutes (range, 150-240 minutes), the mean estimated blood loss was 656 ± 576 mL (range, 100-2000 mL). One patient required transfusion of 2 U of blood, and another required 5 U; both were obese, and access to the prostate gland was more difficult than usual, but this was clearly not related to the presence of the allograft. There was no impairment to bladder descent caused by the presence of the allograft or the ureteroneocystostomy. Urethrovesical anastomosis could be easily performed in all cases in the standard manner, even in the 2 obese patients. The only necessary modification of surgical technique was the avoidance of ipsilateral lymph node dissection (LND), to prevent kidney transplant injuries. Two patients (25%) had bilateral positive prostate biopsies, and in 6 (75%) the positive biopsies were unilateral. In the patients with bilateral positive prostate biopsies, LND yielded seven and three nodes, respectively. In 3 patients LND was performed at the same side as the positive prostate biopsies (four, two, and one lymph node(s), respectively), and in the remaining 3 patients LND was contralateral to the positive prostate biopsies (five, five, and three lymph nodes, respectively). No deterioration of graft function was observed in any case. All patients were followed, and mean follow-up was 11.9 ± 8.4 months (range, 2-30 months). During this time frame PSA was undetectable. All patients but 2 achieved good continence rates: 1 patient uses 2 diapers and the other 2 pads per day.

COMMENT

In the near future the incidence of prostate cancer in renal transplant patients is expected to increase because

of such factors as better survival rates of renal transplant patients and their increasing age at transplantation.[1,4] Most patients (84%) with prostate cancer detected after solid organ transplantation are diagnosed with localized disease.[17] There is controversy regarding the ideal treatment modality for localized prostate cancer in the general (non-transplant) population, and the same occurs with kidney transplant patients. Konety *et al.*,[17] in a retrospective multicenter study, found that the predominant method for treating this disease in solid organ transplant patients was radical prostatectomy. These investigators also concluded that aggressive therapeutic intervention as in the general population yields good results and should be pursued.

Surgical treatment was our preferred method of treatment. Radical prostatectomy can be performed with perineal, retropubic, and laparoscopic approaches. The final decision is based on surgeon expertise. We usually use retropubic access, and our results confirm the idea that it did not represent any additional difficulties to the procedure.

It is known that the presence of lymph node metastasis in men diagnosed with clinically localized prostate cancer portends a poor prognosis.[18] Accurate identification of these men allows more precise prognostication and might have important implications regarding the initiation of adjuvant therapy. Despite advances in noninvasive staging, pelvic LND remains the most accurate means of detecting lymph node metastases in men with clinically localized prostate cancer. In general, it seems reasonable to omit LND in men with a biopsy Gleason sum ≤ 6 and a total PSA value ≤ 10 ng/mL. Ultimately, however, this decision should be made according to physician and patient preference, considering the low contemporary morbidity associated with LND.[19] Because the issue of LND in kidney transplant patients is unresolved, we decided to perform unilateral lymphadenectomy regardless of PSA level and Gleason score.

Hafron *et al.*[20] have advocated that radical perineal prostatectomy should be preferred because of the need of major technical modifications like the different placement of the retractors to position them away from the transplant kidney, a modification that limited mobilization of the peritoneum ipsilateral to the allograft.[21,22] They also concluded that the identification of the transplanted ureter was of utmost importance to avoid injury to it. We believe that a large incision and wide mobilization of the peritoneum is not necessary for adequate retropubic exposure in kidney transplant patients, except perhaps in obese men. In these cases, we simply extend the skin and aponeurosis incision without wide peritoneum mobilization. We usually perform incisions of 10 cm in length. In our series, because the bladder easily reached the urethral stump, identification of the ureteroneocystostomy was not necessary. The retropubic approach is far more familiar to most urologists, which renders the presence of a transplant surgeon unnecessary to treat these patients.

Positive focal margins were seen in 2 patients in our series: in 1 at the apex of the prostate and in the other at the right lateral margin. Even though there were few patients in the present series, the margin positivity rate (2 of 8 patients) is comparable to that in larger radical retropubic prostatectomy series in non-transplanted patients.[23,24]

The modification of immunosuppressive regimens is another unresolved issue. Prostate cancer is a slow-growing tumor in the majority of cases. The differentiation grade of tumors detected in our series, as shown by the Gleason score, was moderate. We decided not to make any modification in the immunosuppressive regimen of our patients and to observe them. Later modification of drug regimens will be done if at all necessary. Because prostate cancer incidence and characteristics vary widely worldwide owing to environmental and racial issues, it would be important to establish a worldwide cancer registry for better defining treatment strategies before and after transplantation.

CONCLUSIONS

In renal transplant recipients with localized prostate cancer, curative treatment should be offered despite the fact that there is no consensus about the best treatment modality in this setting. Kidney transplantation does not interfere with surgical access to the prostate gland. Radical retropubic prostatectomy in renal transplant patients is safe and can be used to effectively treat localized prostate cancer achieving equivalent results to non transplant patients. The only technical modification needed is avoidance of ipsilateral lymphadenectomy.

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