

LOCALIZED PROSTATIC CANCER IN PATIENTS SUBMITTED TO RENAL TRANSPLANT

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ABSTRACT

Objective: An attempt is made to evaluate the incidence of prostate cancer in patients who have previously undergone a kidney transplant surgery and to determine the best therapeutic approach to this target group.

Material and Methods: All kidney transplant male patients over 40 years of age were studied with respect to diseases unrelated to the transplants, which later affected them, mainly focusing on neoplastic disease and, more specifically, prostate cancer.

Results: Of 397 kidney-transplanted patients, 146 (37%) were males, at least 40 years old. Among the 10 of them (6.8%) who developed neoplastic diseases, there were two cases (1.4%) of prostatic cancer. Both were treated with a radical retropubic prostatectomy with no technical difficulty, in spite of the presence of a graft in one of the iliac fossa.

Conclusions: Prostate cancer incidence in kidney transplant patients is still low (1.8%), but it will certainly heighten as transplants are performed in increasingly older people and as better immunosuppressive drugs are introduced to lengthen the survival of grafts and patients. Because these cancers are expected to be more aggressive as a consequence of continuous immunosuppression, early diagnosis is of critical importance, and those patients should be made aware of the need for frequent screening for prostate cancer.

Key words: prostate; prostatic neoplasms; kidney; transplants

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INTRODUCTION

Prostatic cancer represents the most frequent neoplasm in men, but its biologic behavior is anomalous, presenting, more often than not, little aggressiveness. Therefore, its mortality rate is inferior to that of other malignant tumors such as lung and colon cancer (1).

The development of malignant diseases after organ transplants is a well-known complication. Due to multiple factors, prolonged immunosuppression can lead to the emergence of many forms of neoplasm

(2). Race and environment are factors that contribute to the emerging of many tumor types: oriental transplanted patients are more predisposed to digestive tract neoplasm, while occidental ones seem prone to skin cancer (3).

Urogenital tract malignant pathologies occur more frequently in transplanted patients, when compared to the general population, and 34% of non-dermatologic cancers diagnosed in transplanted patients have this localization (4). Curiously, prostatic carcinoma presents lower incidence in transplanted patients than in the general population. In *Cincinnati Transplant Tumor Registry* records, out of 8,191 ma-

Table 1 – Patients’ gender, age and etiology of CRF in kidney recipients.

Group	Number (%)	Etiology of CRF (%)	
Male > 40 years	146 (36.7)	CGN 39 (26.7)	DM 32 (21.9)
Male < 40 years	111 (28)	CGN 40 (36)	DM 26 (23.4)
Female > 40 years	82 (20.7)	CGN 28 (34.1)	DM 16 (19.5)
Female < 40 years	15 (14.6)	CGN 15 (25.8)	DM 12 (20.6)
Total	397 (100)	CGN 122 (30.7)	DM 86 (21.6)

CRF = chronic renal failure; CGN = chronic glomerulonephritis; DM = diabetes mellitus.

lignant tumors cases, only 154 (1.8%) were related to prostatic cancer (4), while its incidence in cancer patients in general reaches 21% (1). This low incidence is probably related to age and survival rate of transplanted patients. However, the observed gradual increase in the average age of transplanted patients as well as the prolonged survival due to the use of new immunosuppressive drugs should result in greater prostatic cancer occurrence in this particular group of male patients.

In the United States, the *United Network for Organ Sharing (UNOS)* recorded, from 1988 to 1993, a raise from 39% to 45% in the number of renal-transplanted patients over 45 years of age (4). The *Brazilian Association of Organ Transplants (BAOT)* records, from 1995 to 2000, 38% renal transplants in patients over 40 years of age (5).

Considering the estimated increase in prostatic cancer incidence in renal-transplanted men and the peculiarities due to the prolonged use of immunosuppressors and to the graft position in one of the iliac fossae, it is important to establish an attendance and follow-up model for this target group.

MATERIALS AND METHODS

From April 1992 to November 2000, 397 renal transplants were performed in our service, 37 of which were double pancreas-kidney transplants. Table-1 shows the causes of renal insufficiency and the donor type, with the patients categorized by sex and age. All male patients over 40 years of age, in addition to a regular clinical exam, were evaluated by an urologist once a year by means of a rectal exam, ultrasonography of the prostate and urinary tract, and PSA. The criteria for biopsy realization were PSA level superior to 4 ng/mL and/or a suspect rectal exam. This group of patients was retrospectively studied in relation to their main pathologies, with emphasis to neoplasms and, in special, to prostatic adenocarcinoma (Table-2).

RESULTS

In Table-1, it can be observed that, out of 397 renal transplants, 257 (65%) were performed in male

Table 2 - Most frequent morbidities of male kidney recipients > 40 years.

Infectious diseases	CMV 71 (48.6%)	UTI 45 (30.8%)	FI 23 (15.7%)
Cardiovascular	SAH 134 (91.7%)	CI 18 (12.3%)	
Neoplasm	10 (6.8%)		

CMV = cytomegalovirus; UTI = urinary tract infection; FI = fungal infection; SAH = systemic arterial hypertension; CI = coronary insufficiency.

Table 3 -Neoplasms in male kidney recipients > 40 years.

Pancreatic cystoadenoma	1
Parathyroid adenoma	1
Spinocelular carcinoma of the skin	2
Kaposi's sarcoma	1
Lymphoma	1
Burkit's lymphoma	1
Prostate adenocarcinoma	1
Total	9

patients; of which 111 (43.2%) were less than 40 years old, while 144 (56.8%) were more than 40 years old. The maximum age in this group was 71 years old and the average age, 51.1 years old. The post-transplant follow-up ranged from 2 to 96 months, with an average of 42 months. Chronic glomerulonephritis (31%) and diabetes mellitus (22%) were the most frequent chronic renal failure etiologies in all groups, without statistic difference among them.

Table-2 describes the main morbidities that affected male transplanted patients who were over 40 years of age and it can be observed that neoplasms occurred in 6.8% of the cases. In Table-3, the tumor types are listed, and it can be observed that, in a group of 147 men, 2 (1.4%) developed prostate cancer. Table-4 shows clinical and surgical data of these patients. Preoperative staging of both was T₁C, with histological grade Gleason 4 (2 + 2). Surgical staging changed to T₂C with Gleason 5 (3 + 2), in case n° 1, while, in case n° 2, there was a reclassification to T₃C (seminal vesicle affected), with Gleason 8 (3 + 5). Both patients were submitted to a radical prostatectomy and, during follow-up (24 months, in case n° 1, and 9 months, in case n° 2), PSA remained inferior to

0.1 ng/mL in both cases. Diagnostic biopsy had been performed 72 months after renal transplant, in case n° 1, and 41 months after, in case n° 2.

DISCUSSION

It is expected that 10% of the male population will be affected by prostate cancer in some period of their lives. Incidence of this neoplasm grows with age advancement, reaching 60% in men over 60 years of age (1,6). Analysis of this data leads us to expect a high incidence of the disease in male patients over forty years of age submitted to renal transplant. However, our statistics reveal only 2 cases (1,4%). Malavaud et al. (7) investigated 120 renal-transplanted men over 50 years of age: 11 (9,2%) presented PSA levels superior to 4 ng/mL and, of these, 9 were biopsed, with 7 (5,8%) having the diagnosis of prostate cancer confirmed. Konety et al. (4), in an investigation undertaken by the *Urologic Society for Transplant and Vascular Surgery*, identified 18 cases by means of questionnaires sent and answered by 60 members of the society. Seven of these eighteen cases were identified among the 2,446 solid organ transplants performed by the Pittsburgh University (4). Kinahan et al. (8) found 30% of prostate adenocarcinoma in specimen obtained from prostate transurethral resection performed in men previously submitted to renal transplant, while, in the general population, T₁ cancer incidence is 10%. Present incidence of prostate cancer in transplanted patients can be related to an inadequate screening, to a low transplant frequency in older men or to a survival insufficiently long for the disease to settle in (4,7,8). With the increase in the number of transplanted patients of more advanced age and the longer survival rate of these patients, the prostatic carcinoma incidence ought to rise.

Table 4 - Clinical data of the 2 prostate cancer cases, both treated with radical prostatectomy.

	Age	Time since transplant	PSA	Clinical stage biopsy	Gleason score in	Surgical stage	Gleason score in surgical specimens	Follow-up (PSA <0.1)
case 1	75	72 months	4.4	T ₁ C	2 + 2	T ₂ C	3 + 2	24m
case 2	57	41 months	10.1	T ₁ C	2 + 2	T ₃ C	3 + 5	9m

Prostate cancer treatment in renal-transplanted patients deserves careful consideration, not only because of a kidney localized in one of the iliac fossae, but also because of the prolonged use of immunosuppressors agents, recognizably cancerigen (9). Our 2 patients were treated with radical prostatectomy, which offers greater possibility of disease eradication with the maintenance of immunosuppression. In both cases, it was chosen a retropubic access without resection of the lymph nodes of the iliac chain from the same side of the graft. Both evolved without any problem and remain continent, though impotent. Radical prostatectomy was also the chosen option in the majority of similar cases described in the literature (4,8,10-12). The more numerous series with 18 patients published by Konety et al. (4) had 15 cases in stage T₂ and three with metastatic disease. Among the patients in stage T₂, 7 had PSA levels above 10 ng/mL, one of which had PSA > 100 ng/mL. Nine (60%) of the T₂ patients were submitted to a radical prostatectomy, 3 (20%) were treated with radiotherapy, 2 (13,5%) were only clinically followed, and 1 (6,5%), with PSA > 100 ng/mL, treated with androgenic suppression. Of the three patients with metastatic disease, two were submitted to orchiectomy and one was treated with a LH-RH analog.

As for radical prostatectomy, the majority of the authors prefers retropubic access and maintains intact the iliac lymphatic chain from the same side of the transplanted kidney (4,7,11,12). Yiu et al. (10) defend the perineal access, discussing that the bladder and the iliac fossa must not be damaged, so avoiding any lesion to the transplanted kidney and the ureterovesical anastomosis. Based in our two case experience and in the reports by many authors, we think that the choice criterion for the surgical access should mainly consider the surgeon's experience and preferences.

Treatment with external radiotherapy was contraindicated by almost all of the authors (7,11,12). Radiotherapy can potentially promote eradication of the cancerigen prostatic cells, but there are reports in the literature of disease recurrence in up to 50% of the cases, when follow-up extends for more than five years (13). In the case of renal-transplanted patients, radiotherapy presents one more inconvenience – the possibility of actinic nephritis occurrence (14). In the

three cases reported by Konety et al. (4) that were treated by external radiotherapy, 6,500 cGy of external radiation were used with protection of the graft. After a forty-month follow-up, two patients remained alive, with stable PSA levels, and one died from non-reported causes (4).

The prognosis for such patients is difficult to define, for two reasons: few reported cases in the literature and the need of immunosuppression maintenance. The 2 cases reported in our research had a follow-up inferior to 2 years, which does not allow for any sound conclusion regarding evolution and prognosis. Konety et al. (4), in a more numerous series with a longer follow-up, suggest that prostate cancer in transplant patients manifests itself in a more aggressive way. After a 30 month follow-up, of the 9 patients with localized disease and treated with radical prostatectomy, 4 (44%) were alive, showing no evidence of disease, 3 (33%) evolved with metastasis, 1 (11%) died of lung cancer and one (11%) did not have a follow-up.

With the expected increase in the incidence of prostate cancer in transplanted patients and the theoretically greater aggressiveness this tumor manifests in this group of male patients, early diagnosis and immediate treatment should provide a more favorable prognosis. PSA dosage and rectal exam are the most effective detection methods of prostatic adenocarcinoma. Earlier publications suggested that PSA would be higher in patients on hemodialysis, since this protein is not eliminated during filtration. However, Morton et al. (15) studying the possible alterations in the PSA in patients on dialytic treatment and in immunosuppressed patients after renal transplant, did not find significative difference as compared to the general population. Malavaud et al. (7), based exclusively on PSA level greater than 4 ng/mL in transplanted patients indicated for biopsy, confirmed cancer diagnosis in 77% of the cases. In our 2 cases, the main indication for biopsy was an abnormal evolution of the PSA.

CONCLUSIONS

The screening for prostate adenocarcinoma performed in 146 men over 40 years of age and bear-

ers of renal graft allowed the diagnosis of 2 cases (1,4%). It is probable, however, that this rate of incidence will rise due to a more frequent performance of transplants on chronic renal patients over 40 years of age and an increase in the life expectancy of such patients. The therapeutic strategy for prostatic neoplasm in this group of patients must consider the greater aggressiveness of this disease and the need of its eradication so that the immunosuppression is maintained. In localized cancer cases, radical prostatectomy is the strategy that best achieves this objective and the retropubic access can be performed without technical difficulty, in spite of the presence of the kidney in one of the iliac fossae.

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