BJU Int 2024 doi:10.1111/bju.16558

Original Article

BJUI
BJU International

Prostate cancer and solid organ transplantation: patient management and outcomes

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Objective

To analyse the management and outcomes of individuals diagnosed with prostate cancer either before or after organ transplantation, as the impact of organ transplantation and associated immunosuppression on the incidence, progression, and mortality of prostate cancer remains an area of substantial clinical interest and uncertainty.

Patients and Methods

We conducted a retrospective analysis of patients from two tertiary care centres who had solid organ transplantation and were diagnosed with prostate cancer before or after organ transplantation. Data collected included demographics and clinical information.

Results

The cohort consisted of 110 patients with a median (interquartile range [IQR]) age at prostate cancer diagnosis of 62 (56.6–67.2) years and a median (IQR) age at transplantation of 58.6 (52.7–65.3) years. Renal transplantation was the most common (54%). The median (IQR) prostate-specific antigen concentration at prostate cancer diagnosis was 6.2 (4.5–10) ng/mL, and the distribution of American Urological Association risk groups was: low risk, 36%; intermediate risk, 50%; and high risk, 14%. In all, 45 (41%) patients were diagnosed with prostate cancer prior to transplantation. Management included radical prostatectomy (RP; 62%), prostate radiotherapy (RT; 13%), and active surveillance (AS; 18%). During a median (IQR) follow-up of 5.8 (2.5–10) years from prostate cancer diagnosis, one (2%) patient developed metastatic disease. In all, 65 (59%) patients were diagnosed with prostate cancer subsequent to organ transplantation. Management included AS (29%), RT (45%), and RP (15%). During a median (IQR) follow-up of 5.3 (1–8.4) years, three patients (5%) developed metastatic disease. There were no deaths from prostate cancer.

Conclusion

A diagnosis of localised prostate cancer should not preclude solid organ transplantation, and the presence of a transplant does not appear to substantially impact risk of prostate cancer progression.

Keywords

prostate cancer, solid organ transplantation, active surveillance, radical prostatectomy, radiotherapy

Introduction

Recipients of solid organ transplants traverse a unique medical landscape profoundly influenced by immune modulation—a balance designed to forestall graft rejection while potentially reshaping susceptibilities to cancer development. As the frequency of solid organ transplantation increases [1], the transplant recipient demographic advances in age, and the incidence of prostate cancer among this population rises [2].

Extant evidence suggests the incidence and progression rates of prostate cancer remain unaltered by preceding solid organ transplantation and immunosuppression [3]. Previous investigations have not revealed elevated prostate cancer-specific mortality rates among patients with transplants

when compared with broader immunocompetent patients with prostate cancer [4,5]. Additionally, prior research attests to the safety and efficacy of surgical and radiotherapeutic interventions in patients after transplantation [2,5,6] and has not revealed an escalated risk for aggressive prostate cancer among patients after transplantation [7].

Nonetheless, the nexus between immunosuppression in solid organ transplant recipients and the susceptibility for prostate cancer remains unclear, with an absence of definitive guidelines [2], although a recent multidisciplinary consensus statement is available to guide management [8].

Our objective was to evaluate pre- or post-transplant individuals diagnosed with prostate cancer, analyse their management and outcomes, and help understand whether standard recommendations warrant continuation or modification. We hypothesised that cancer-specific outcomes for patients with localised prostate cancer in the setting of solid organ transplantation would be similar to broader population-level prostate cancer outcomes.

Patents and Methods

This retrospective study utilised the database of patients with prostate cancer and patients who underwent organ transplantation from the University of Chicago and the University of Michigan Medical Centers. The inclusion criteria encompassed all males diagnosed with prostate cancer who underwent organ transplantation either before or after their prostate cancer diagnosis.

Following Institutional Review Board approvals and waiver of informed consent, we collected demographic data, including the age at the time of prostate cancer diagnosis, age at transplantation, the type of organ transplanted, AUA/National Comprehensive Cancer Network (NCCN) prostate cancer risk category, PSA levels, International Society of Urological Pathology (ISUP) Grade Group, primary treatment for prostate cancer, and follow-up information, encompassing salvage treatment, biochemical recurrence (BCR), metastatic disease, and mortality.

Descriptive statistics consisted of medians and interquartile ranges (IQRs) for continuous variables and proportions for categorical variables. Patients were monitored until either mortality occurred or lost to follow-up. For those who were lost to follow-up before experiencing mortality, their data were censored on the day of their last recorded follow-up. All tests of significance were two-sided, and $P < 0.05$ was deemed statistically significant. We conducted all statistical analyses using the Statistical Package for the Social Sciences (SPSS®), version 25.0 (IBM Corp., Armonk, NY, USA).

Results

Entire Cohort

There were 110 patients included in the overall cohort. The median (IQR) age at prostate cancer diagnosis was 62 (56.6–67.2) years, while the median (IQR) age at the time of transplantation was 58.6 (52.7–65.3) years. Among our cohort, 57 (52%) were White/Caucasian and 49 (44.5%) Black. Notably, 59 (53.6%) patients received kidney transplants, 27 (24.5%) underwent heart transplants, 13 (11.8%) received liver transplants, and five (4.5%) received lung transplants (Table 1). At the time of prostate cancer diagnosis, the median (IQR) PSA concentration was 6.2 (4.5–10) ng/mL.

Patients were stratified into risk categories following the AUA/NCCN guidelines [9,10], resulting in 39 (35.5%) low-

Table 1 Patients' characteristics.

Characteristic	Prostate cancer prior to solid organ transplantation (*n* = 45)	Solid organ transplantation prior to prostate cancer diagnosis (*n* = 65)
Age at prostate cancer diagnosis, years, median (IQR)	57.7 (53.6–62.8)	65.8 (59.7–69.2)
Age at transplantation, years, median (IQR)	61.7 (57–67)	57.5 (50–63.5)
Time from prostate cancer diagnosis to transplantation, years, median (IQR)	4.7 (2–6.8)	
Time from transplantation to prostate cancer diagnosis, years, median (IQR)		7.3 (3.6–11.8)
PSA at prostate cancer diagnosis, ng/mL, median (IQR)	5.5 (4.1–7)	6.8 (4.8–10.7)
Race, *n* (%)		
White/Caucasian	24 (53)	33 (51)
Black/African American	20 (44)	29 (45)
Hispanic	0	2 (3)
Asian/Mideast Indian	0	1 (1.5)
Other	1 (2)	0
Solid organ transplanted, *n* (%)		
Kidney	27 (60)	32 (49)
Heart	10 (22)	17 (26)
Lung	3 (7)	2 (3)
Liver	5 (11)	8 (12)
Kidney and heart	0	2 (3)
Kidney and liver	0	2 (3)
Kidney and pancreas	0	1 (1.5)
Pancreas	0	1 (1.5)

Table 2 Cancer characteristics and treatments.

Variable	Prostate cancer prior to solid organ transplantation (*n* = 45)	Solid organ transplantation prior to prostate cancer diagnosis (*n* = 65)
Age at prostate cancer treatment, years, median (IQR)	60.2 (53–61.8)	66.3 (61.2–70.2)
Highest Grade Group on prostate biopsy, *n* (%)		
1	23 (51)	24 (37)
2	19 (42)	17 (26)
3	2 (4.4)	12 (19)
4	1 (2.2)	4 (6)
5	0	8 (12)
Clinical stage at prostate cancer diagnosis, *n* (%)		
T1a	0	2 (3)
T1b	0	1 (1.5)
T1c	37 (82)	54 (83)
T2a	6 (13)	5 (8)
T2b	1 (2)	1 (1.5)
T2c	0	2 (3)
Unknown	1 (2)	0
Prostate cancer risk classification, *n* (%)		
Low	20 (44)	19 (29)
Intermediate	22 (49)	33 (51)
High	3 (7)	13 (20)
Primary treatment, *n* (%)		
RP	28 (62)	9 (14)
RT	5 (11)	19 (29)
AS	8 (18)	19 (29)
RP + ADT	0	1 (1.5)
RT + ADT	2 (5)	12 (18.5)
ADT only	1 (2)	1 (1.5)
Cryoablation	0	1 (1.5)
Radical cystectomy	1 (2)	0
Watchful waiting	0	2 (3)

risk, 55 (50%) intermediate-risk, and 16 (14.5%) high-risk cases. Initial treatment modalities included radical prostatectomy (RP) for 38 (34.5%) patients, radiotherapy (RT) with or without androgen-deprivation therapy (ADT) for 35 (31.8%) patients, and active surveillance (AS) for 27 (24.5%) patients (Table 2).

The immunosuppression regimen for most patients who underwent kidney transplantation remained consistent throughout the study period and typically included tacrolimus, mycophenolate, and prednisone, with basiliximab (Simulect®; Novartis pharmaceuticals, Basel, Switzerland) or thymoglobulin used for induction. A few patients who underwent transplantation earlier in the study period were on a different regimen consisting of cyclosporine, azathioprine, and prednisone. For patients who underwent heart transplantation, the most common immunosuppression regimen comprised mycophenolate, tacrolimus, and prednisone. For patients who underwent lung transplantation, the most common immunosuppression regimen was tacrolimus, mycophenolate, and prednisone. In patients who underwent liver transplantation, there was greater variability, with regimens ranging from cyclosporine alone, tacrolimus alone, to tacrolimus combined with mycophenolate or azathioprine.

Patients Diagnosed with Prostate Cancer Prior to Transplantation

Within our cohort, 45 (41%) patients were diagnosed with prostate cancer before undergoing transplantation. The median (IQR) age at prostate cancer diagnosis was 57.7 (53.6–62.8) years, while the median (IQR) age at transplantation was 61.7 (57–67) years. The median (IQR) interval between prostate cancer diagnosis and transplantation was 4.7 (2.0–6.8) years (Table 1). However, this time interval was influenced by various factors, including the clinical need for the transplant, the patient's underlying condition and overall health, the time spent on the transplant waiting list, and other factors related to the transplantation process. Notably, only one patient (2%) experienced a delay in his transplantation due to prostate cancer.

Further stratifying by risk, we found the median (IQR) time from prostate cancer diagnosis to transplantation was 3 (1.0–5.5) years for low-risk patients, 5.1 (2.3–10) years for intermediate-risk patients, and 8.9 (6.0–12.7) years for high-risk patients. The distribution of transplant types included 27 (60%) kidney transplants, 10 (22%) heart transplants, five (11%) liver transplants, and three (7%) lung transplants. The median (IQR) PSA concentration at prostate cancer diagnosis was 5.5 (4.1–7) ng/mL (Table 1).

The patients' treatment stratified by prostate cancer risk category is detailed in Table 3. In the low-risk category, one (5%) patient underwent radical cystectomy for concurrent muscle-invasive bladder cancer and one (5%) patient was treated with ADT only. Notably, the patient treated with ADT had a PSA concentration of 6.7 ng/mL during his transplant evaluation, had Grade Group 1 involving 20% of a single core and 5% in another core, and was recommended a conservative course of management to avoid surgery or RT. ADT was stopped shortly after diagnosis due to decreased libido and the patient passed away aged 73 years from causes unrelated to prostate cancer.

None of the patients in the AS group converted to active treatment during the follow-up period. A total of five of 28 patients who initially underwent RP developed BCR, comprising four patients with intermediate-risk and one with high-risk prostate cancer. The median time from RP to BCR was 4.3 (2.4–110 years (Table 4).

One patient with intermediate-risk prostate cancer developed metastatic disease during the follow-up period. This patient

Table 3 Prostate cancer treatments stratified by risk.

Prostate cancer risk classification	Primary prostate cancer treatment	Prostate cancer prior to solid organ transplantation (*n* = 45)	Solid organ transplantation prior to prostate cancer diagnosis (*n* = 65)
Low risk, *n* (%)	RP	9 (45)	2 (11)
	RT	2 (10)	4 (21)
	AS	7 (35)	12 (63)
	Cryoablation		1 (5)
	ADT only	1 (5)	
	Radical cystectomy	1 (5)	
Intermediate risk, *n* (%)	RP	18 (86)	5 (16)
	RT	2 (9)	12 (37)
	RT + ADT		6 (19)
	AS	1 (5)	6 (19)
	Watchful waiting		2 (6)
	ADT only		1 (3)
High risk, *n* (%)	RP	1 (33)	2 (15)
	RP + ADT		1 (8)
	RT		3 (23)
	RT + ADT	2 (67)	6 (46)
	AS		1 (8)

Table 4 Follow-up and cancer outcomes.

Variable	Prostate cancer prior to solid organ transplantation (*n* = 45)	Solid organ transplantation prior to prostate cancer diagnosis (*n* = 65)
Follow-up, years, median (IQR)	5.8 (2.5–10)	5.3 (1–8.4)
Progression on AS, *n* (%)	0	4 (6)
BCR following RP, *n* (%)	5 (11)	1 (1.5)
Salvage treatment, *n* (%)		
RT	2 (4)	0
RT + ADT	1 (2)	1 (1.5)
Abiraterone + ADT	0	1 (1.5)
Metastatic progression, *n* (%)	1 (2)	3 (4.6)
Death, *n* (%)	13 (29)	22 (34)
Death related to prostate cancer, *n* (%)	0	0

was diagnosed aged 54 years, underwent RP with pathology indicating Grade Group 2, T3aN0 disease, with extraprostatic extension and positive right posterolateral margins. He experienced BCR 4.3 years after surgery and received salvage RT. After an additional 6 years and at a PSA concentration of 1 ng/mL, he started ADT for 2.5 years. He had his kidney transplant at the age of 68 years, 2 years and 9 months after discontinuing ADT. He developed oligometastatic disease: solitary rib lesion, soft tissue inter-costal space and sacral lesion, which were treated with stereotactic body RT (SBRT) 21 months following renal transplantation. This patient is still alive with a functioning renal allograft, 15 months since SBRT.

During a median (IQR) follow-up time of 5.8 (2.5–10) years from prostate cancer diagnosis, one patient (2%) developed metastatic disease, and 13 (29%) patients died, yielding a 5-year overall survival rate of 86%. None of the recorded death were attributed to prostate cancer (Table 4).

Patients with a Transplant Prior to Prostate Cancer Diagnosis

There were 65 (59%) patients who received transplants before being diagnosed with prostate cancer. These patients had a median (IQR) age at transplantation of 57.5 (50–63.5) years and median (IQR) age at prostate cancer diagnosis of 65.8 (59.7–69.2) years. The median time between transplantation and prostate cancer diagnosis was 7.3 (3.6–11.80 years (Table 1).

When stratified by risk, we observed median (IQR) times from transplantation to prostate cancer diagnosis of 5.6 (2.5–12.8) years for low-risk patients, 7.5 (5.0–10.6) years for intermediate-risk patients, and 7.8 (2.2–12) years for high-risk patients. In this group, 33 (51%) were White, and 29 (45%) were Black. Kidney transplants were most common, with 32 (49%), followed by heart transplants in 17 (26%), liver transplants in eight (12.3%), and lung transplant in two (3%). The median (IQR) PSA concentration at prostate cancer diagnosis was 6.8 (4.8–10.7) ng/mL (Table 1).

The patients' treatments stratified by prostate cancer risk category are detailed in Table 3.

Within the AS group, four of 19 converted to active treatment during the follow-up period: one with low-risk

prostate cancer, two with intermediate-risk, and one with high-risk prostate cancer. One patient with high-risk prostate cancer who was initially treated with RP had BCR (Table 4).

None of the patients diagnosed with prostate cancer following their solid organ transplantation had any changes to their immunosuppression regimen as a result of the prostate cancer diagnosis.

Three patients developed metastatic disease during the follow-up period. The first patient was diagnosed with *de novo* metastatic prostate cancer shortly after renal transplantation at the age of 68 years. He had a PSA concentration of 25 ng/mL, Grade Group 4 on prostate biopsy and sclerotic pelvic bone lesions on bone scan. He was treated with ADT alone and died 2 years following has prostate cancer diagnosis due to severe sepsis and multi-organ failure originating from leg cellulitis. The second patient, who had a liver transplant at the age of 59 years, was diagnosed with prostate cancer at the age of 65 years. He had a PSA concentration of 10 ng/mL and Grade Group 5 on prostate biopsy. His initial treatment involved RT + ADT, with the addition of abiraterone during the follow-up period due to metastatic disease that he developed 2 years after his prostate cancer diagnosis. The third patient received both kidney and liver transplants at the age of 58 years. He was diagnosed with prostate cancer at the age of 66 years, with a PSA concentration of 4.6 ng/mL and high-volume Grade Group 3 on prostate biopsy. He underwent primary prostate RT and experienced metastatic disease after 4 years. He died of other causes 6 years after diagnosis.

During a median (IQR) follow-up time of 5.3 (1–8.4) years, three (4.6%) patients developed metastatic disease, and 22 (34%) patients died, yielding an overall 5-year survival rate of 88%. None of the recorded deaths were attributed to prostate cancer (Table 4).

Discussion

The interplay between solid organ transplantation and prostate cancer has gained more prominence as transplant recipient demographics evolve and transplantation procedures become more common. While prostate cancer is a prevalent malignancy in the general population, there is longstanding debate regarding its management in solid organ transplantation, both candidates being considered for and those diagnosed after transplantation.

Our retrospective study, encompassing 110 patients from the University of Chicago and the University of Michigan, offers insights into the dynamics of prostate cancer in transplant recipients. We observed the median time from prostate cancer diagnosis to transplantation was 4.7 years, although our dataset lacks precise information regarding the interval between prostate cancer diagnosis and the patient's placement on the transplant waiting list. Among the men with early stage prostate cancer managed with AS, there were no adverse cancer-related events before or after transplantation, suggesting this is a safe strategy. Among those treated for prostate cancer prior to solid organ transplantation, only one developed metastatic disease. Therefore, our data supports managing patients with prostate cancer, who are candidates for solid organ transplantation, in line with current AUA [9] and NCCN [10] guidelines.

The median time from transplantation to the development of prostate cancer was 7.3 years, emphasising the potential importance of vigilant long-term monitoring [11]. Among patients who underwent AS, there were lower rates of transformation to active treatment comparing to general cohorts without a transplant [12,13], validating this approach in appropriate patients. Among all patients diagnosed with prostate cancer following transplantation, there were four patients who developed metastatic disease although two of them had either no prostate cancer screening or a rising PSA over a few years and a significant delay prior to diagnosis.

It is noteworthy the distribution of transplantation types in our cohort is diverse, with kidney transplantation being the most common (54%). This heterogeneity is unique to the present cohort, as it includes heart, liver, and lung transplants, in contrast to other publications that primarily focus on prostate cancer in renal transplant recipients [5]. It is unknown whether different immunosuppression regimens variably impact incidence rates or natural history of prostate cancer.

Of particular interest are patients diagnosed with prostate cancer before transplantation, as much of the literature primarily addresses cases that develop prostate cancer after transplantation. For those diagnosed before transplantation, our findings reveal a diverse range of risk categories and management choices. Notably, this subgroup in our cohort did not show any disease progression under AS [14] and had relatively low BCR rates following RP (11%) [15], affirming the appropriateness of adhering to established standards of care for localised prostate cancer, even when organ transplantation is planned. AS should be strongly considered for many of these patients. Our data highlights those individuals diagnosed with high-risk prostate cancer experienced prolonged intervals between their prostate cancer diagnosis and transplantation. Given the previously discussed favourable outcomes, it becomes imperative to emphasise the importance of avoiding unnecessary delays or refusals in transplantation for high-risk patients. However, it is crucial to acknowledge that the causes behind these delays may be linked to the selected treatment approach. This correlation is exemplified in a recent French study involving 216 patients diagnosed with prostate cancer during the evaluation for renal transplantation. The study revealed that RT was

associated with the lengthiest delay between prostate cancer diagnosis and transplantation, whereas AS exhibited the shortest delay [16]. Overall, a nuanced approach is essential for patients with higher-volume intermediate- or high-risk disease, considering many factors including life expectancy, comorbidities, expected time to transplantation, and urinary and erectile status [8].

Conversely, patients who received transplants before a prostate cancer diagnosis present a unique challenge. The median time between transplantation and prostate cancer diagnosis in our cohort (7.3 years) is similar to prior studies [17]. Importantly, only 20% of patients in this subgroup developed high-risk prostate cancer, aligning with the risk profile seen in the general population [7]. This underscores that a prior transplantation does not appear to predispose a patient to a higher risk of developing aggressive prostate cancer. Although fewer intermediate- (five patients) and high-risk (three patients) patients in this subgroup underwent RP, likely due to comorbidities, our findings affirm that RP following organ transplantation is a viable option [18]. A retrospective multi-institutional study performed a matched comparison between renal transplant recipients and non-renal transplant recipients undergoing RP for non-metastatic prostate cancer and showed a higher estimated blood loss, length of stay, and time to catheter removal in renal transplant recipients; however, no differences were shown in complications and prostate cancer outcomes [19]. In our study only one of the patients in this subgroup experienced BCR after surgery. The rate of transformation to active treatment from AS (four out of 19 patients) is concordant with published rates in cohorts with immunocompetent patients [12,13]. Our cohort also include one high-risk patient who may not have been a candidate for AS if not for his prior organ transplant.

Our study identified only four (3.6%) cases of metastatic progression, a relatively low rate, particularly as two of those had sub-optimal prostate cancer screening, and none of the cohort's deaths were attributed to prostate cancer. This suggests that, when diagnosed in transplant recipients, prostate cancer does not appear to exhibit more aggressive behaviour or lead to worse outcomes compared to the general population [4]. Importantly, three of the four cases of metastatic disease were diagnosed following transplantation, highlighting the need for continued vigilance in post-transplant monitoring. We might suggest screening for high microsatellites instability and DNA mismatch repair deficiencies in post-transplant patients with high-risk prostate cancer, as these settings have shown an interaction between T lymphocytes and tumour microenvironment and treatment efficacy with pembrolizumab [20,21]. The possibility does exist, although seems unlikely based on available literature and our study, that immunosuppression can initiate cancer progression in a subset of patients.

A recent consensus statement including solid organ transplant and genitourinary cancer specialists suggest that patients with prostate cancer being considered for transplantation should be managed in accordance with established standards of care, emphasising that almost all patients with localised prostate cancer should not be excluded from transplantation or undergo a cancer-related delay until solid organ transplantation [8]. Our data supports this statement as none of the deaths in our cohort was related to prostate cancer. The prostate cancer can either be monitored, if appropriate, or undergo treatment, either before or after transplantation [4,22]. For cases presenting with very high-risk localised or metastatic disease, a nuanced decision-making process is advocated, one that weighs factors such as life expectancy and other medical conditions [8].

There are several limitations associated with our data. Primarily, our cohort has a retrospective nature, originating from two referral centres. This introduces potential variabilities in surveillance protocols and decision-making processes, as decisions for these patients are occasionally made in multidisciplinary forums. Additionally, the time points for measurement extend to and from the actual transplantation surgery rather than from the time when patients were initially placed on the transplantation waiting lists. Additionally, our study only included patients who received a transplant and did not report on patients with prostate cancer who were denied transplantation or who died while on the waiting list prior to receiving a transplant.

In conclusion, our data suggest the management of prostate cancer before or after solid organ transplantation should align with established guidelines for the general prostate cancer population and emphasises that almost all patients with localised prostate cancer should not be excluded from transplantation or undergo a prostate cancer-related delay.

Acknowledgements

None.

Disclosure of Interests

All authors declare no conflict of interest.

Funding

None.

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Abbreviations: ADT, androgen-deprivation therapy; AS, active surveillance; BCR, biochemical recurrence; IQR, interquartile range; NCCN, National Comprehensive Cancer Network; RP, radical prostatectomy; (SB)RT, (stereotactic body) radiotherapy.

