

Delaying Kidney Transplantation in Patients With Prostate Cancer: Is It Warranted?



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Kidney transplant recipients are at increased risk of de novo malignancy following transplantation, believed to be related at least in part to immunosuppression.^{1,2} Furthermore, immunosuppressive medications can affect

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the progression of malignancies following transplantation.³ Based on these facts, society guidelines recommend delaying kidney transplantation in patients with end-stage kidney disease (ESKD) and malignancy.⁴ However, malignancies have different rates of progression and mortality risk, and delaying kidney transplantation in patients with ESKD is associated with a higher risk of death.⁵ Therefore, the decision to delay kidney transplantation in kidney transplant candidates should involve a comparison of the mortality risk from the malignancy itself to the likelihood of death associated with remaining dialysis-dependent, a risk that is estimated to be 55% at 5 years based on the 2019 US Renal Data System Atlas.⁶ This issue is highlighted in kidney transplant candidates with prostate cancer given the following: (1) prostate cancer has a 98% 5-year relative survival for all stages combined⁷ and (2) risk of prostate cancer after transplantation is not increased, suggesting that immunosuppression does not affect its risk.⁸ Therefore, delaying transplantation may not be warranted. This is the question that Sarabu et al⁹ attempt to answer in their study published in this issue of *Kidney Medicine*.

In their retrospective study, Sarabu et al⁹ included male, dialysis-dependent Medicare beneficiaries from the 2019 US Renal Data System database between the ages of 40 years and 79 years who did not have a documented diagnosis of prostate cancer at the time of dialysis initiation. Using 1:1 propensity-based risk-set matching, they matched 15,554 patients treated with dialysis with prostate cancer to those without prostate cancer. They found that patients treated with dialysis with prostate cancer had an 11% higher likelihood of death at 5 years than those without prostate cancer, although the absolute risk difference was only 3% (33% vs 30%, respectively). They also found that prostate cancer in patients treated with dialysis was associated with a 22% lower chance of receiving a kidney transplant. Perhaps their most important finding was that kidney transplantation was associated with an 80% improvement in survival in ESKD patients compared with those remaining on dialysis, regardless of the presence or absence of prostate cancer.

The study findings should not be interpreted that all patients with ESKD and prostate cancer will have a

mortality benefit from kidney transplantation and thus should receive a kidney transplant. Rather, the study needs to be interpreted in the context of several important limitations. First, the retrospective observational study design, despite matching, can be associated with differences in unmeasured confounders between the study groups that may affect outcomes. Second, the study used registry data, the quality of which depends on the completeness and accuracy of the submitted data. Third, registry data lack granularity in important aspects related to prostate cancer that may affect outcomes such as staging, Gleason score, and treatment received. Therefore, even though the study found no difference in cancer-specific mortality between patients treated with dialysis with and without prostate cancer, prostate cancer-specific mortality and the modifying effect of stage and treatment cannot be evaluated. It is likely that most patients who received a kidney transplant had a less aggressive form of prostate cancer, which is an important selection bias that would tilt the results in favor of transplantation. Lastly, the findings of the study cannot be generalized to patients who are diagnosed with prostate cancer before the initiation of dialysis, since these patients were excluded from the analysis.

Despite these limitations, the study findings of the potential benefit of kidney transplantation in this group of patients add to the scarce literature in this area and support more recent society guidelines suggesting that kidney transplantation likely does not have to be delayed for patients with ESKD and low-grade prostate cancer. The American Society of Transplantation 2020 guidelines recommend no wait time for patients with very low-risk disease, low-risk disease, or low-volume intermediate-risk disease managed with active surveillance or those with high-volume intermediate-risk disease, high-risk disease, or very high-risk disease with <10% predicted 15-year mortality if treatment is initiated.⁴ The KDIGO (Kidney Disease: Improving Global Outcomes) clinical practice guideline on the evaluation and management of candidates for kidney transplantation recommends that kidney transplant candidates with prostate cancer and Gleason score of ≤ 6 can be listed for transplantation and that no wait time is needed for those curatively treated for prostate cancer with Gleason score of ≤ 6 .¹⁰ However, KDIGO does not provide a clear recommendation regarding the wait time for patients managed with active surveillance. Guidelines from other major societies are summarized in [Table 1](#).^{11,12}

Many guidelines have based their recommendations on the largest cohort of pre-solid organ transplant patients with prostate cancer, which comes from the Israel Penn

Table 1. Society Guidelines for Kidney Transplantation in Patients With End-Stage Kidney Disease and Prostate Cancer

Society	Recommendation	Year
American Society of Transplantation ⁴	<ul style="list-style-type: none"> • No wait time for patients with very low-risk disease, low-risk disease, or low-volume intermediate-risk disease managed with active surveillance or those with high-volume intermediate-risk disease, high-risk disease, or very high-risk disease with <10% predicted 15-y mortality if treatment is initiated • A 2-y wait time is recommended for patients with metastatic castration-sensitive disease • No listing for patients with metastatic castration-resistant disease 	2020
Kidney Disease: Improving Global Outcomes ¹⁰	<ul style="list-style-type: none"> • No listing for patients with active malignancy excluding those with low-grade malignancies such as prostate cancer with Gleason score of ≤6 • No wait time for patients who were curatively treated for prostate cancer with Gleason score of ≤6 	2020
European Association of Urology ¹¹	<ul style="list-style-type: none"> • No wait time for patients with appropriately treated low stage/grade prostate cancer 	2019
European Renal Best Practices ¹²	<ul style="list-style-type: none"> • Wait time to be determined after discussion with an oncologist taking into account the patient's age, comorbid conditions, and potential for cancer progression or recurrence 	2013

International Transplant Tumor registry and included only 90 patients (77 of whom were kidney transplant candidates).¹³ Patients were diagnosed with prostate cancer at a median of 19 months before transplantation; of these patients, 88% had stage I or II disease, and the treatment was not known in 40% of patients. Patients were followed for a median of 20.5 months following transplantation, during which recurrent prostate cancer developed in 18% of patients at a median of 10.6 months following transplantation. Higher rates of recurrence (36.4% vs 14.3%-15.9%, respectively) and mortality (27.3% vs 2.9%-6.8%, respectively) were found in those with stage III disease than those with stage I-II disease. Interestingly, the lowest risk of recurrence (13.0%) was noted in those with a wait time of <2 years, and the highest mortality (16.7%) was noted in those with a wait time of >5 years.

The second-largest study of pretransplant ESKD patients with prostate cancer included all recipients of the first kidney transplant in Norway from 1963 to 2010 stratified by pretransplant malignancy status.¹⁴ There were 377 patients with pretransplant malignancy (only 43 of whom had prostate cancer) and 5,296 without pretransplant malignancy included in the study. At a median follow-up of 6.8 years, there were no differences in all-cause mortality or cancer-related mortality between kidney transplant recipients with and without a history of prostate cancer before transplantation. Longer wait periods were not associated with a lower risk of all-cause mortality or cancer-related mortality in this study.

Other notable studies have shown no recurrence following prostatectomy in a small cohort of pretransplant patients with low- and intermediate-risk prostate cancer,¹⁵ no increased risk of prostate cancer recurrence in patients treated with dialysis who receive a kidney transplant compared with those who remain on dialysis,¹⁶ and no increase in cancer-specific mortality in kidney transplant

recipients with prostate cancer compared with propensity score-matched control patients with prostate cancer but without a solid organ transplant.¹⁷ Despite the paucity and limitations of the literature on the topic, the risk of recurrence in kidney transplant candidates with low- and intermediate-risk prostate cancer seems low and may not be associated with a significant increase in cancer-specific or all-cause mortality.

Despite current guidelines, program-specific practices vary widely across transplant centers in the United States with regard to transplant eligibility for kidney transplant candidates with prostate cancer.¹⁸ A study surveying 90 surgeons from 65 transplant centers across the United States found that definitive treatment (eg, radical prostatectomy, brachytherapy) was required for transplant eligibility in 45% of survey responders but depended on disease risk in the remaining 55%. The most common wait time between prostate cancer treatment and transplant eligibility was 2 years but varied widely across centers.¹⁸

In summary, the study by Sarabu et al⁹ adds evidence of the potential benefit of kidney transplantation in dialysis-dependent men with prostate cancer but needs to be interpreted with the caveats listed above. Published data on prostate cancer recurrence and outcomes following kidney transplantation remain limited and are lacking in granular data stratifying patient outcomes by disease stage, treatment, and wait time before transplantation. More data are needed to risk stratify patients in this group to determine the optimal wait time before transplantation (if any) and which patients are likely to benefit the most from kidney transplantation.

ARTICLE INFORMATION

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