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Increased risk of postoperative in-hospital complications after radical prostatectomy in patients with prior organ transplant

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Abstract

Background: To analyze postoperative, in-hospital, complication rates in patients with organ transplantation before radical prostatectomy (RP).

Methods: From National Inpatient Sample (NIS) database (2000–2015) prostate cancer patients treated with RP were abstracted and stratified according to prior organ transplant versus nontransplant. Multivariable logistic regression models predicted in-hospital complications.

Results: Of all eligible 202,419 RP patients, 216 (0.1%) underwent RP after prior organ transplantation. Transplant RP patients exhibited higher proportions of Charlson comorbidity index ≥2 (13.0% vs. 3.0%), obesity (9.3% vs. 5.6%, both $p < 0.05$), versus to nontransplant RP. Of transplant RP patients, 96 underwent kidney (44.4%), 44 heart (20.4%), 40 liver (18.5%), 30 (13.9%) bone marrow, <11 lung (<5%), and <11 pancreatic (<5%) transplantation before RP. Within transplant RP patients, rates of lymph node dissection ranged from 37.5% (kidney transplant) to 60.0% (bone marrow transplant, $p < 0.01$) versus 51% in nontransplant patients. Regarding in-hospital complications, transplant patients more frequently exhibited, diabetic (31.5% vs. 11.6%, $p < 0.001$), major (7.9% vs. 2.9%) cardiac complications (3.2% vs. 1.2%, $p = 0.01$), and acute kidney failure (5.1% vs. 0.9%, $p < 0.001$), versus nontransplant RP. In multivariable logistic regression models, transplant RP patients were at higher risk of acute kidney failure (odds ratio [OR]: 4.83), diabetic (OR: 2.81), major (OR: 2.39), intraoperative (OR: 2.38), cardiac (OR: 2.16), transfusion (OR: 1.37), and overall complications (1.36, all $p < 0.001$). No in-hospital mortalities were recorded in transplant patients after RP.

Conclusions: Of all transplants before RP, kidney ranks first. RP patients with prior transplantation have an increased risk of in-hospital complications. The highest risk, relative to nontransplant RP patients appears to acute kidney failure.

KEYWORDS
bone barrow, heart, kidney, liver, surgical complications

1 | INTRODUCTION

Prostate cancer (PCa) treatment in patients with immunosuppression due to prior organ transplantation is challenging. For example, in kidney transplant PCa patients radiation therapy may irreparably harm the graft and lead to radiation-induced ureteral stenosis.[1] No current guidelines recommend optimal treatment of PCa in transplant recipients. However, several case reports, single institutional studies, and two reviews investigated the safety and feasibility of radical prostatectomy (RP) in kidney transplant patients.[2–7] Moreover, a recent meta-analysis by Hevia et al. combined 41 studies from 1991 to 2018 with PCa treatment after kidney transplantation ($n = 319$). Of all, 262 underwent RP and the numbers of patients within included studies ranged from 1 to 29.[3,8,9] Conversely, very few studies and case reports focused on RP after other transplantations than kidney.[10–15] For example, Beyer et al. reported about five liver and heart transplant patients treated with RP.[10] In consequence, little is known about complications after RP in transplant PCa patients and data rely on small institutional series with few observations.

We addressed this void and relied on a contemporary large-scale epidemiological database, namely the National Inpatient Sample (NIS) 2000–2015. We hypothesized that in-hospital complications in transplant RP patients are significantly higher than in nontransplant patients. Moreover, we postulated that the concept of RP in transplant patients has gained importance in recent years.

2 | MATERIAL AND METHODS

2.1 | Data source and study population

We relied on the NIS database (2000–2015) that includes approximately 20% of US inpatient hospitalizations, with discharge abstracts from eight million hospital stays. The NIS is a set of longitudinal hospital inpatient databases included in the Healthcare Cost and Utilization Project family, created by the Agency for Healthcare Research and Quality through a Federal-state partnership.[16] Within the NIS, we identified all ≥18 years old patients with a primary diagnosis PCa international classification of diseases, ninth revision, clinical Modification (ICD-9-CM code 185.0), and who underwent RP (ICD-9-CM code 60.4, 60.5, and 60.62). Patients were stratified according to transplant (ICD-9 code V42.1, V42.2, V42.7, V42.6, V.42.81, V42.83) versus no transplant status.

2.2 | Statistical analysis

Descriptive statistics included frequencies and proportions for categorical variables. Means, medians, and interquartile ranges (IQRs) were reported for continuously coded variables. The χ^2 tested the statistical significance in proportions' differences. The t test and Kruskal–Wallis test examined the statistical significance of means' and distributions' differences.

In the first set of analyses, we tabulated results according to transplant versus no transplant RP patients. Subsequently, we tabulated results according to different kinds of transplantation: heart versus kidney versus lung versus liver versus bone marrow. Due to sample size limitations in lung transplant ($n = 4$) and pancreatic transplant ($n = 2$) patients, no tabulation could be performed.

In the second set of analyses, we focused on early postoperative outcomes, namely, in-hospital complications. Complications rates were defined using secondary ICD-9 diagnostic codes, as previously described.[17] Postoperative complications consisted of in-hospital death, parenteral nutrition, vascular, wound, transfusions, infectious, cardiac, gastrointestinal, pulmonary, diabetic, genitourinary, intraoperative, major, and overall complications. Moreover, it consisted of acute kidney failure and miscellaneous medical and surgical.[18] Univariable, as well as multivariable logistic regression models tested the effect of prior transplant on in-hospital complications. Covariates consisted of age at diagnosis, Charlson comorbidity index (CCI), insurance status, annual hospital volume (defined as lowest vs. medium vs. highest tertial), hospital bedsize (small vs. medium vs. large [according to NIS guidelines and depending on its region]), region of residence, surgical approach (robotic vs. open), lymph node dissection status. Additionally, adjustment was made for clustering. Finally, differences in RP rates over time in transplant patients were estimated with estimated annual percent change (EAPC) that relied on log-linear methodology, as previously reported.[19–21] All tests were two sided with a level of significance set at $p < 0.05$ and R software environment for statistical computing and graphics (version 3.4.3) was used for all analyses.

3 | RESULTS

3.1 | Descriptive characteristics of the study population

Of all eligible 202,419 RP patients (2000–2015), 216 (0.1%) underwent RP after prior organ transplantation, between 2000 and 2015 (Table 1). Median age and length of stay were, respectively, 67 versus 67 years and 2 versus 2 days for transplant versus nontransplant RP patients (both $p \geq 0.2$). Patients with RP after organ transplantation exhibited higher proportions of CCI ≥ 2 (13.0 vs. 3.0, $p < 0.001$), metabolic syndrome (11.1 vs. 4.1, $p < 0.001$), obesity (9.3% vs. 5.6%, $p = 0.03$), relative to nontransplant RP counterparts. Moreover, transplant RP patients, were more frequently treated in hospitals with high annual volume (47.2% vs. 33.6%, $p < 0.001$) and large bedsize (75.9% vs. 68.0%, $p = 0.04$). Additionally, transplant RP patients were frequently more often nonhome-based discharged

TABLE 1 Descriptive characteristics of 216 transplant patients who underwent radical prostatectomy versus 202,203 nontransplant radical prostatectomy patients, diagnosed within the National Inpatient Sample database from 2000 to 2015

Variable		No transplant (*n* = 202,203) (99.9%)	Transplant (*n* = 216) (0.1%)	*p* value
Age at diagnosis, years	Median (IQR)	62 (57–67)	62 (57–66)	0.5
Length of stay, days	Median (IQR)	2 (1–3)	2 (1–3)	0.2
Hospital costs, $	Median (IQR)	25,929 (16,677–39,172)	32,141 (20,773–44,906)	<0.001
Transplant type	Bone marrow		30 (13.9)	
	Heart		44 (20.4)	
	Kidney		96 (44.4)	
	Liver		40 (18.5)	
	Lung		<11 (<5.0)	
	Pancreatic		<11 (<5.0)	
CCI	0–1	196,196 (97.0)	188 (87.0)	<0.001
	≥2	6007 (3.0)	28 (13.0)	
Obese	Yes	11,328 (5.6)	20 (9.3)	0.028
Metabolic syndrome	Yes	8371 (4.1)	24 (11.1)	<0.001
Smoking	Yes	17,193 (8.5)	<11 (<5.0)	0.031
Surgical approach	Open	131,787 (65.2)	143 (66.2)	1
	Robotic	54,411 (26.9)	59 (27.3)	
Lymph node dissection	Yes	103,186 (51.0)	108 (50.0)	0.8
Hospital annual volume	Low	66,508 (32.9)	36 (16.7)	<0.001
	Medium	67,802 (33.5)	78 (36.1)	
	High	67,893 (33.6)	102 (47.2)	
Disposition	Home-based	95,293 (47.1)	112 (51.9)	<0.01
	Nonhome-based	5265 (2.6)	14 (6.5)	
	Unknown	101,645 (50.3)	90 (41.7)	
Density	Rural	1399 (0.7)	<11 (<5.0)	0.9
	Urban	31,627 (15.6)	30 (13.9)	
Race/ethnicity	Caucasian	125,964 (62.3)	118 (54.6)	<0.01
	African American	19,379 (9.6)	35 (16.2)	
	Other/unknown	56,860 (28.1)	63 (29.2)	
Insurance	Medicare	62,877 (31.1)	108 (50.0)	<0.001
	Medicaid	3848 (1.9)	<11 (<5.0)	
	Private	126,957 (62.8)	92 (42.6)	
	Other	8521 (4.2)	<11 (<5.0)	
Income	First quartile	36,222 (17.9)	36183 (17.9)	1
	Second to fourth quartile	166,197 (82.1)	166020 (82.1)	
Teaching status	Teaching	126,784 (62.7)	186 (86.1)	<0.001
	Nonteaching	75,419 (37.3)	30 (13.9)	
Hospital bedsize	Small	21,763 (10.8)	19 (8.8)	0.043
	Medium	42,848 (21.2)	33 (15.3)	
	Large	137,592 (68.0)	164 (75.9)	

TABLE 1 (Continued)

Variable		No transplant (n = 202,203) (99.9%)	Transplant (n = 216) (0.1%)	p value
Region	Midwest	49,451 (24.5)	46 (21.3)	0.016
	Northeast	38,013 (18.8)	57 (26.4)	
	South	72,730 (36.0)	64 (29.6)	
	West	42,009 (20.8)	49 (22.7)	

Abbreviations: CCI, Charlson comorbidity index; IQR, interquartile range.

(6.5% vs. 2.6%, $p < 0.01$) and also insurance status significantly differed, relative to nontransplant RP patients ($p < 0.001$). Median hospital costs were 32,141 versus 25,929$ for transplant versus nontransplant RP patients, respectively ($p < 0.001$). Conversely, no statistically significant or clinically meaningful differences were observed between the surgical approach (robotic: 27.3% vs. 26.9%, $p = 1$), lymph node dissection status (50.0% vs. 51.0%, $p = 0.8$) or income.

Of all 216 transplant RP patients, 96 underwent kidney (44.4%), 44 heart (20.4%), 40 liver (18.5%), 30 (13.9%) bone marrow, 4 lung (1.9%), and 2 pancreatic (0.9%) transplantation before RP. Within transplant RP patients (Table 2), median age at diagnosis ranged from 60 (kidney transplant) to 65 (heart transplant) years ($p = 0.02$). No differences were observed between different transplant RP patients according to surgical approach, length of in-hospital stay, hospital costs, CCI, obesity, or nonhome-based discharge (all $p \geq 0.1$). Conversely, rates of lymph node dissection ranged from 37.5% (kidney transplant) to 60.0% (bone marrow transplant, $p < 0.01$) versus 51.0% for nontransplant patients.

3.2 | In-hospital complications: Transplant versus nontransplant RP patients

Important differences according to in-hospital complications were observed between transplant versus nontransplant RP patients (Table 3). Specifically, transplant patients more frequently exhibited cardiac (3.2% vs. 1.2%, $p = 0.01$), diabetic (31.5% vs. 11.6%, $p < 0.001$), and major complications (7.9% vs. 2.9%, $p < 0.001$), relative to nontransplant RP patients. Moreover, transplant patients more frequently exhibited acute kidney failure (5.1% vs. 0.9%, $p < 0.001$), compared to their nontransplant RP counterparts. No differences were observed between transplant versus nontransplant RP patients according to other types of complications (vascular, wound, infectious, gastrointestinal, pulmonary, genitourinary, intraoperative, all $p > 0.05$), overall complications (14.8% vs. 10.8%, $p = 0.069$) or in-hospital mortality (0% vs. 0.1%, $p = 1$).

3.3 | In-hospital complications: Differences in transplant RP patients

We also made important observations according to in-hospital complications of RP patients with different transplant types (Table 4). Specifically, cardiac complications only occurred in kidney transplant RP patients (7.3% vs. 0% vs. 0 vs. 0%, $p = 0.035$), relative to heart, liver, and bone marrow RP patients. Conversely, gastrointestinal complications only occurred in liver (7.5%) and heart (6.8%) transplant RP patients and not in kidney or bone marrow RP patients (both 0%, $p = 0.03$). No differences were observed between different transplant RP patients according to other types of complications (vascular, wound, infectious, pulmonary, genitourinary, intraoperative, diabetic, acute kidney failure), as well as according to major and overall complications rates (all $p \geq 0.2$).

3.4 | Logistic regression models testing in-hospital complications between transplant versus nontransplant RP patients

In multivariable logistic regression models adjusted for covariates and clustering (Table 5), previous transplant represented an independent predictor of overall complications (odds ratio [OR]: 1.36, confidence interval [CI]: 1.13–1.63), major complications (OR: 2.39, CI: 1.86–3.02), cardiac (OR: 2.16, CI: 1.49–3.02), diabetic (OR: 2.81, CI: 2.41–3.27), transfusion (OR: 1.37, CI: 1.11–1.69), intraoperative complications (OR: 2.38, CI: 1.50–3.57, all $p < 0.001$), and acute kidney failure (OR: 4.83, CI: 3.54–6.42, $p < 0.01$). Moreover, previous transplant were independently predicted with nonhome disposition (OR: 1.51, CI: 1.12–1.99, $p < 0.01$). In sensitivity analyses that excluded kidney transplant RP patients ($n = 120$, 55.6%), previous transplant independently predicted acute kidney failure (OR: 4.30, CI: 2.75–6.42, $p < 0.001$), relative to nontransplant patients.

3.5 | Trends over time in transplant RP patients

Regarding trends over time of transplant RP patients important observations were made between the study period from the year 2000 to 2015. Specifically, an EAPC of 4.1% ($p = 0.04$) was observed. The lowest number of transplant RP patients was observed in the year 2005 ($n < 11$) and highest number in the years 2008, 2011, and 2014 ($n = 21$). A plateau of an average amount of 15 RPs in transplant patients was observed since the year 2006 onward.

TABLE 2 Descriptive characteristics of 30 bone marrow versus 44 heart versus 96 kidney versus 40 liver transplant patients who underwent radical prostatectomy diagnosed within the National Inpatient Sample database from 2000 to 2015

Variable		Kidney (n = 96)	Heart (n = 44)	Liver (n = 40)	Bone marrow (n =30)	p value
Age at diagnosis, years	Median (IQR)	60 (56–65)	65 (61–67)	62 (57–67)	60 (55–63)	0.02
Length of stay, days	Median (IQR)	2 (2–3)	2 (2–4)	2 (1–4)	2 (1–2)	0.6
Hospital costs, $	Median (IQR)	31,202 (20,596–44,204)	31,705 (16,892–46,729)	35,027 (21,843–48,702)	30,706 (21,377–39,344)	0.6
CCI	0–1	84 (87.5)	39 (88.6)	31 (77.5)	29 (96.7)	0.12
	≥2	12 (12.5)	<11	<11	<11	
Obese	Yes	12 (12.5)	<11	<11	<11	0.5
Metabolic syndrome	Yes	13 (13.5)	<11	<11	<11	0.3
Surgical approach	Open	68 (70.8)	27 (61.4)	28 (70)	18 (60.0)	0.5
	Robotic	26 (27.1)	11 (25.0)	<11	11 (36.7)	
Lymph node dissection	Yes	36 (37.5)	25 (56.8)	27 (67.5)	18 (60.0)	<0.01
Hospital annual volume	Low	19 (19.8)	<11	<11	<11	0.07
	Medium	30 (31.2)	21 (47.7)	<11	15 (50.0)	
	High	47 (49.0)	20 (45.5)	23 (57.5)	<11	
Disposition	Home-based	47 (49)	18 (40.9)	26 (65.0)	15 (50.0)	0.5
	Nonhome-based	<11	<11	<11	<11	
	Unknown	43 (44.8)	22 (50)	12 (30)	13 (43.3)	
Density	Rural	0 (0)	0 (0)	0 (0)	<11	<0.01
	Urban	<11	<11	12 (30.0)	<11	
Race/ethnicity	Caucasian	38 (39.6)	25 (56.8)	26 (65)	24 (80.0)	<0.001
	African American	28 (29.2)	<11	<11	0 (0)	
	Other/unknown	30 (31.2)	15 (34.1)	11 (27.5)	<11	
Insurance	Medicare	49 (51)	30 (68.2)	18 (45.0)	<11	0.017
	Medicaid	<11	<11	<11	<11	
	Private	38 (39.6)	11 (25.0)	19 (47.5)	21 (70.0)	
	Other	<11	0 (0)	<11	<11	
Income	1st quartile	17 (17.7)	<11	<11	<11	0.6
	2nd–4th quartile	79 (82.3)	37 (84.1)	30 (75.0)	26 (86.7)	
Teaching status	Teaching	83 (86.5)	41 (93.2)	34 (85)	22 (73.3)	0.12
	Nonteaching	13 (13.5)	<11	<11	<11	
Hospital bedsize	Small	<11	<11	<11	<11	0.3
	Medium	19 (19.8)	<11	<11	<11	
	Large	68 (70.8)	37 (84.1)	32 (80.0)	23 (76.7)	
Region	Midwest	15 (15.6)	<11	14 (35.0)	<11	0.14
	Northeast	24 (25.0)	14 (31.8)	<11	<11	
	South	37 (38.5)	<11	11 (27.5)	<11	
	West	20 (20.8)	13 (29.5)	<11	<11	

Abbreviations: CCI, Charlson comorbidity index; IQR, interquartile range.

TABLE 3 In-hospital complications of 216 transplant patients who underwent radical prostatectomy versus 202,203 non-transplant radical prostatectomy patients, diagnosed within the National Inpatient Sample database from 2000 to 2015

Variable	No transplant	Transplant	*p* value
In-hospital death, %	0.1	0	1
Vascular complications, %	0.4	0	0.6
Parenteral nutrition, %	0.1	0.5	0.6
Wound complications, %	0.3	0.9	0.2
Transfusion complications, %	8.2	10.2	0.3
Infectious complications, %	0.2	0.2	1
Cardiac complications, %	1.2	3.2	0.01
Gastrointestinal complications, %	4.3	2.8	0.4
Pulmonary complications, %	1.7	2.3	0.7
Diabetic complications, %	11.6	31.5	<0.001
Genitourinary complications, %	1.0	1.4	0.8
Acute kidney failure, %	0.9	5.1	<0.001
Intraoperative complications, %	1.0	1.9	0.3
Major complications, %	2.9	7.9	<0.001
Overall complications, %	10.8	14.8	0.069
Miscellaneous medical, %	5.4	7.4	0.2
Miscellaneous surgical, %	2.3	3.7	0.3

4 | DISCUSSION

We hypothesized in-hospital complications in transplant RP patients are significantly higher than in nontransplant RP patients. Our analyses resulted in several noteworthy observations.

First, we made important observations regarding transplant RP patients. Specifically, we found that only 216 patients underwent RP after prior organ transplantation in an observation period from 2000 to 2015. Moreover, we observed that RP patients with prior transplantation are different from nontransplant RP patients. Specifically, RP transplant patients had higher CCI at PCa diagnosis and were more frequently obese and had metabolic syndrome. Moreover, RP in transplant patients resulted in significantly higher hospital costs. Our findings are in an agreement with the previous meta-analysis by Hevia et al., where 41 kidney transplant PCa studies were included (the year 1991–2018) pooling 262 RP treated patients, where number of included patients ranged from 1 to 29.[8] In consequence, RP in transplant patients is a rarely performed procedure. However, it is not surprising that RP transplant patients were more obese, frequently displayed the metabolic syndrome, and were sicker than nontransplant RP patients, since a commonly known side effect of immunosuppression for transplant patients is metabolic syndrome and obesity.[22–24]

Second, we also made important observations regarding differences in baseline characteristics between different transplant types before RP patients. Specifically, we found that the majority of transplant RP patients are kidney transplant PCa patients (44%), followed by heart (20%), liver (19%), and bone marrow (14%) in that order. Lung (2%) and pancreatic (1%) transplant PCa patients are exceptions in this population-based study. These proportions differ from the general distribution of organ transplantation, which are worldwide 67% kidney, 22% liver, 5.6% heart, 4.0% lung, and 1.8% pancreas.[25] Moreover, transplant RP patients differed according to age PCa at diagnosis that ranged from 60 (kidney and bone marrow transplant) to 65 years (heart transplant). Additionally, rates of lymph node dissection rates were lowest in kidney transplant (37.5%) RP patients, relative to all other transplant RP patients (at least ≥57%), versus 50% in nontransplant patients. Compared to previous studies, in a European tertiary care center of RP excellence, in an observation period of 22 years (1992–2013), RPs were performed in 20 kidney, 5 liver, and 5 heart transplant patients. Also here, heart transplant patients were the oldest in this cohort.[10] However, no rates of lymph node dissection status were reported in this study. In a study by Kleinclauss et al. that relied on 20 kidney transplant RP patients, only 50% received lymph node dissection and of those had 50% a unilateral lymph node dissection.[6] These observations are not surprising since the transplanted kidney is located in the iliac fossa and, therefore, and prevents safe ipsilateral lymph node dissection.[6,10,26–29]

Third, we made important observations regarding in-hospital complications in transplant RP patients relative to nontransplant RP patients. Specifically, we observed that cardiac (3.2% vs. 1.2%), diabetic (31.5% vs. 11.6%) and major complications (7.9% vs. 2.9%) are more frequent in transplant RP, relative to nontransplant RP patients. Similarly, transplant patients more frequently exhibited acute kidney failure (5.1% vs. 0.9%). Moreover, in multivariable logistic regression models, prior transplant was independently associated with higher rates of overall and major complications, as well as cardiac, diabetic, transfusion, and intraoperative complications, as well as acute kidney failure. Moreover, prior transplant was independently associated with nonhome disposition. It is particular of interest that acute kidney failure was the most pronounced in-hospital complication in transplant RP patients, even when kidney transplant patients were excluded. To the best of our knowledge, no previous publication focused on in-hospital complications and their rates in transplant RP patients, with adjustment for baseline patient and hospital characteristics. Moreover, important sample size limitations applied to all previous publications focusing on RP after transplant. In consequence, all previously reported data about in-hospital complications in RP transplant patients can be descripted as individual patients' case reports. For example, in the study by Beyer et al., four and one patients of the 20 included kidney transplant patients received a blood transfusion (Clavien Dindo II) or had a lymphocele (Clavien Dindo IIIa).[10] Moreover, in the meta-analysis of Hevia et al., of 262 RP treated kidney transplant patients, 13% had postoperative compilations of which 1.9% were Clavien Dindo ≥III.[8]

TABLE 4 In-hospital complications of 96 kidney versus 44 heart versus 40 liver versus 30 bone marrow transplant patients who underwent radical prostatectomy diagnosed within the National Inpatient Sample database from 2000 to 2015

Variable	Kidney	Heart	Liver	Bone marrow	*p* value
Parenteral nutrition, %	1.0	0	0	0	0.8
Wound complications, %	0	0	2.5	3.3	0.2
Transfusion complications, %	8.3	13.6	10.0	13.3	0.8
Infectious complications, %	0	0	2.5	0	0.2
Cardiac complications, %	7.3	0	0	0	0.035
Pulmonary complications, %	3.1	2.3	2.5	0	0.8
Diabetic complications, %	30.2	36.4	32.5	23.3	0.7
Genitourinary complications, %	2.1	2.3	0	0	0.7
Acute kidney failure, %	5.2	4.5	10.5	0	0.3
Gastrointestinal complications, %	0	6.8	7.5	0	0.025
Intraoperative complications, %	3.1	0	2.5	0	0.5
Major complications, %	8.3	6.8	12.5	3.3	0.6
Overall complications, %	16.7	13.6	22.5	3.3	0.16
Miscellaneous medical, %	6.2	9.1	15.0	0	0.11
Miscellaneous surgical, %	4.2	2.3	5.0	3.3	0.9

TABLE 5 Univariable and multivariable logistic regression models predicting in-hospital complications for transplant versus nontransplant radical prostatectomy patients after adjustment for age at diagnosis, Charlson comorbidity index, insurance status, income, annual hospital volume, hospital bedsize, region, approach (open vs. robotic), and lymph node dissection

	Univariable		Multivariable	
No transplant versus transplant RP patients	OR (CI)	*p* value	OR (CI)	*p* value
	Ref	-	Ref	-
Overall complications	1.44 (0.97–2.07)	0.055	1.36 (1.13–1.63)	<0.001
Major complications	2.83 (1.66–4.51)	<0.001	2.39 (1.86–3.02)	<0.001
Cardiac complications	2.85 (1.21–5.60)	<0.01	2.16 (1.49–3.02)	<0.001
Diabetes complications	3.50 (2.61–4.64)	<0.001	2.81 (2.41–3.27)	<0.001
Pneumological complications	1.35 (0.48–2.95)	0.5	1.47 (0.95–2.15)	0.063
Wound complications	3.69 (0.61–11.54)	0.066	1.68 (0.56–3.76)	0.3
Transfusion complications	1.27 (0.80–1.93)	0.3	1.37 (1.11–1.69)	<0.01
Genitourinary complications	1.46 (0.36–3.83)	0.5	1.37 (0.78–2.22)	0.2
Gastrointestinal complications	0.64 (0.25–1.32)	0.3	0.69 (0.46–1.00)	0.059
Intraoperative complications	1.90 (0.59–4.47)	0.2	2.38 (1.50–3.57)	<0.001
Acute kidney failure (all transplant patients)	5.85 (3.00–10.24)	<0.001	4.83 (3.54–6.42)	<0.001
Acute kidney failure (without kidney transplant patients)	5.74 (2.24–11.97)	<0.001	4.30 (2.75–6.42)	<0.001
Disposition (nonhome)	2.26 (1.24–3.81)	<0.01	1.51 (1.12–1.99)	<0.01

Abbreviations: CI, confidence interval; OR, odds ratio; RP, radical prostatectomy.

Finally, we also made important observations according to in-hospital complications in the comparison between different transplant RP patients. Specifically, cardiac complications only occurred in kidney transplant RP patients and may be related to the higher prevalence of metabolic syndrome and may increase the risk of long-term renal failure in these patients. Conversely, gastrointestinal complications only occurred in liver and heart transplant RP patients. No differences were observed between different transplant RP patients according to other kinds of complications. To the best of our knowledge, we are the first to report specific in-hospital complication comparison between different transplant RP patients. Unfortunately, these observations rely on small sample sizes. In consequence, our

data cannot be directly compared to previous smaller sample size publications. However, our data suggest that different organ transplantations before RP result in different risk profiles that have to be taken into account, when transplant patients are counseled about RP and eventually undergo RP.

Taken together, our findings demonstrate that transplant RP patients differ from nontransplant RP patients. Specifically, transplant RP patients are sicker and more frequently harbor metabolic syndrome and obesity. Also, within transplant RP patients, differences were observed. Specifically, kidney transplant recipients were most prevalent, followed by heart, liver, and bone marrow transplant patients. Important differences were observed according to age at initial PCa diagnosis and lymph node dissection status. According to in-hospital complications after RP, transplant patients are at higher risk for in-hospital complications in absolute terms and also after multivariable adjustment for patient and baseline characteristics, relative to nontransplant RP patients. Predominant in-hospital complication is acute kidney failure. Finally, no deaths were recorded in transplant patients after RP.

Our work has limitations and should be interpreted in the context of its retrospective and population-based design. Moreover, complications were limited to in-hospital rates and not standardized according to a validated classification system (e.g., Clavien Dindo). In consequence, delayed complications, as well as the readmission rates, could not be examined. Moreover, it could be possible that complication rates reflect additional complications that originated from other causes than RP. Additionally, lack of information on tumor characteristics, such as PCa stage and grade, made it unfortunately impossible to report and account for these important baseline tumor characteristics. Moreover, no information was available on survival outcomes of transplant RP patients in the NIS. Finally, we relied on an inclusion period until 2015. Ideally, our findings should be further validated with more recent databases.

5 | CONCLUSIONS

Of all transplants before RP, kidney ranks first. RP patients with prior transplantation have an increased risk of in-hospital complications. The highest risk, relative to nontransplant RP patients appears to acute kidney failure.

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DATA AVAILABILITY STATEMENT

All data generated for this analysis were from the SEER 18 database. The code for the analyses will be made available after request.

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REFERENCES

1. Mouzinuzin M, Bachaud J-M, Kamar N, et al. Three-dimensional conformal radiotherapy for localized prostate cancer in kidney transplant recipients. *Transplantation*. 2004;78(10):1496-1500.
2. Heidenreich A, Pfister D, Thissen A, Piper C, Porres D. Radical retropubic and perineal prostatectomy for clinically localised prostate cancer in renal transplant recipients. *Arab J Urol*. 2014;12(2):142-148.
3. Narváez A, Suarez J, Riera L, Castells-Esteve M, Cocera R, Vigués F. Our experience in the management of prostate cancer in renal transplant recipients. *Actas Urol Esp*. 2018;42(4):249-255.
4. Minami K, Harada H, Sasaki H, Higuchi H, Tanaka H. Robot-assisted radical prostatectomy in a second kidney transplant recipient. *J Endourol Case Rep*. 2020;6(4):540-543.
5. Marra G, Dalmasso E, Agnello M, et al. Prostate cancer treatment in renal transplant recipients: a systematic review. *BJU Int*. 2018;121(3):327-344.
6. Kleinclauss FM, Neuzillet Y, Tillou X, et al. Morbidity of retropubic radical prostatectomy for prostate cancer in renal transplant recipients: multicenter study from Renal Transplantation Committee of French Urological Association. *Urology*. 2008;72(6):1366-1370.
7. Breyer BN, Whitson JM, Freise CE, Meng MV. Prostate cancer screening and treatment in the transplant population: current status and recommendations. *J Urol*. 2009;181(5):2018-2025.
8. Hevia V, Boissier R, Rodríguez-Faba Ó, et al. Management of localised prostate cancer in kidney transplant patients: a systematic review from the EAU Guidelines on Renal Transplantation Panel. *Eur Urol Focus*. 2018;4(2):153-162.
9. Wagener N, Nyarangi-Dix JN, Teber D, Zeier M, Hohenfellner M. Applicability of robot-assisted laparoscopic radical prostatectomy in renal allograft recipients. *Transplant Proc*. 2012;44(5):1287-1292.
10. Beyer B, Mandel P, Michl U, et al. Oncological, functional and perioperative outcomes in transplant patients after radical prostatectomy. *World J Urol*. 2016;34(8):1101-1105.
11. Singh I, Patel BN, Thohan V, Hemal AK. Robot-assisted laparoscopic radical prostatectomy after heart transplantation. *Urol Ann*. 2013;5(1):56-58.
12. Thompson RH, Leibovich BC, Karnes RJ, Bergstralh EJ, Blute ML. Radical retropubic prostatectomy in immunosuppressed transplant recipients. *J Urol*. 2008;179(4):1349-1352.
13. Tillou X, Chiche L, Guleryuz K, Hervé S, Bensadoun H, Doerfler A. Prostate carcinoma in liver transplant recipients: think about it!. *Urol Oncol*. 2015;33(6):265.e9-13.
14. Reiter WJ, Mock K. Radical prostatectomy for localized prostate cancer in a liver transplant recipient. *Urol Int*. 2005;74(1):95-96.
15. Bayne A, Barry JM, Garzotto M. Radical retropubic prostatectomy after orthotopic liver transplantation. *Urology*. 2005;65(1):175.
16. HCUP-US NIS Overviewhttps://www.hcup-us.ahrq.gov/nisoverview.jsp; 2021.
17. Mazzone E, Preisser F, Nazzani S, et al. The effect of lymph node dissection in metastatic prostate cancer patients treated with radical prostatectomy: a contemporary analysis of survival and early postoperative outcomes. *Eur Urol Oncol*. 2019;2(5):541-548.
18. Yu HY, Hevelone ND, Lipsitz SR, et al. Comparative analysis of outcomes and costs following open radical cystectomy versus robot-assisted laparoscopic radical cystectomy: results from the US Nationwide Inpatient Sample. *Eur Urol*. 2012;61:1239-1244.

19. Wenzel M, Würnschimmel C, Ruvolo CC, et al. Increasing rates of NCCN high and very high-risk prostate cancer versus number of prostate biopsy cores. *Prostate*. 2021;81(12):874-881. https://doi.org/10.1002/pros.24184
20. Würnschimmel C, Kachanov M, Wenzel M, et al. Twenty-year trends in prostate cancer stage and grade migration in a large contemporary german radical prostatectomy cohort. *Prostate*. 2021;81(12):849-856. https://doi.org/10.1002/pros.24181
21. Wenzel M, Nocera L, Collà Ruvolo C, et al. Racial/ethnic disparities in tumor characteristics and treatments in favorable and unfavorable intermediate risk prostate cancer. *J Urol*. 2021;206(1):69-79. https://doi.org/10.1097/JU.0000000000001695
22. Cigrovski Berkovic M, Virovic-Jukic L, Bilic-Curcic I, Mrzljak A. Post-transplant diabetes mellitus and preexisting liver disease–a bidirectional relationship affecting treatment and management. *World J Gastroenterol*. 2020;26(21):2740-2757.
23. Becchetti C, Dirchwolf M, Banz V, Dufour J-F. Medical management of metabolic and cardiovascular complications after liver transplantation. *World J Gastroenterol*. 2020;26(18):2138-2154.
24. Matas AJ, Vock DM. Prednisone-free maintenance immunosuppression in obese kidney transplant recipients. *Clin Transplant*. 2019;33(10):e13668.
25. Mahillo B, Carmona M, Alvarez M, et al. Worldwide distribution of solid organ transplantation and access of population to those practices. *Transplantation*. 2018;102:S71-S72. https://doi.org/10.1097/01.tp.0000542650.33995.b3
26. Fahlenkamp D, Schönberger B, Türk J, Loening SA. Experiences with laparoscopic lymphocele drainage. *Urologe A*. 1994;33(4):336-341.
27. Sun G-H, Fu Y-T, Wu C-J, Chang S-Y. Povidone-iodine instillation for management of pelvic lymphocele after pelvic lymphadenectomy for staging prostate cancer. *Arch Androl*. 2003;49(6):463-466.
28. Domagala P, van den Berg T, Tran K, et al. Surgical safety and efficacy of third kidney transplantation in the ipsilateral iliac fossa. *Ann Transplant*. 2019;24:132-138.
29. Hagen ME, Pugin F, Bucher P, Fasel J, Markar S, Morel P. Robotic kidney implantation for kidney transplantation: initial experience. *J Robot Surg*. 2010;4(4):271-276.

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