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Prostate Cancer

Radical Prostatectomy for Nonmetastatic Prostate Cancer in Renal Transplant Recipients: Outcomes for a Large Contemporary Cohort and a Matched Comparison to Patients Without a Transplant

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Abstract

Background and objective: It is unknown whether renal transplant receipt (RTR) status can affect perioperative and oncological outcomes of radical prostatectomy (RP). Our aim was to evaluate oncological and functional outcomes of RTR patients treated with RP for cN0M0 prostate cancer (PCa) via comparison with a no-RTR cohort.

Methods: RTR patients who had undergone RP at seven European institutions during 2001–2022 were identified. A multi-institutional cohort of no-RTR patients treated with RP during 2004–2022 served as the comparator group. Propensity score matching (PSM) at a ratio of 1:4 was used to match no-RTR patients to the RTR cohort according to age, prostate-specific antigen, and final pathology features. We used Kaplan-Meier plots and multivariable Cox, logistic, and Poisson log-linear regression models to test the outcomes of interest.

Key findings and limitations: After PSM, we analyzed data for 102 RTR and 408 no-RTR patients. RTR patients experienced higher estimated blood loss (EBL), longer length of hospital stay (LOS) and time to catheter removal, higher postoperative complication rates, and a lower continence recovery rate (all $p < 0.001$). On multivariable analyses,

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RTR independently predicted unfavorable operative time (odds ratio [OR] 1.22, 95% confidence interval [CI] 1.18–1.25), LOS (OR 1.57, 95% CI 1.32–1.86), EBL (OR 2.24, 95% CI 2.18–2.30), and time to catheter removal (OR 1.93, 95% CI 1.68–2.21), but not complications or continence recovery. There were no significant differences for any oncological outcomes (biochemical recurrence, local or systemic progression) between the RTR and no-RTR groups. While no PCa deaths were recorded, the overall mortality rate was significantly higher in the RTR group (17% vs 0.5%, $p < 0.001$).

Conclusions and clinical implications: Although RP is feasible for RTR patients, the procedure poses non-negligible surgical challenges, with longer operative time and LOS and higher EBL, but no major differences in terms of complications and continence recovery. The RTR group had similar oncological outcomes to the no-RTR group but significantly higher overall mortality related to causes other than PCa. Therefore, careful selection for RP is required among candidates with previous RTR.

Patient summary: Removal of the prostate for prostate cancer is possible in patients who have had a kidney transplant, and cancer control outcomes are comparable to those for the general population. However, transplant patients have a higher risk of death from causes other than prostate cancer and the prostate surgery is likely to be more challenging.

1. Introduction

The annual number of kidney transplants performed in Europe and the USA is increasing. In addition, the life expectancy for patients with renal transplant receipt (RTR) has significantly improved in recent decades, and is now almost 20 yr for recipients in their fifties [1–5]. As prostate cancer (PCa) remains the most frequent non-skin solid neoplasm for men, a rise in PCa diagnoses is likely among RTR patients [4–7].

Interestingly, several aspects of PCa management in these patients remain to be understood. First, oncological outcomes may be influenced by the immunosuppression regimen [3,8]. Second, whether radical prostatectomy (RP) is appropriate or is associated with a higher risk of complications in comparison to standard cases is a matter of debate because of indirect immunosuppression effects (eg, infections and a lower rate of healing), the anatomic location of the graft, and previous abdominal surgery. Third, RTR patients generally represent a comorbid population with shorter life expectancy [4,5]. Recent evidence suggests excellent long-term outcomes for localized PCa [9], including some high-risk cases, so further evaluation of the potential benefits of active treatment in the RTR population is required [8,10].

Two systematic reviews suggested no major differences for RTR patients with PCa mainly treated with RP [3,11]. Population-based case-control series also mirrored single- or multi-institutional series, but revealed lower overall survival rates for RTR patients [12,13]. Nonetheless, current evidence from non–population-based RP cohorts relies on <500 patients [3,11].

Our group previously investigated overall PCa outcomes for RTR patients using different treatment modalities [8], including robotic surgery [14] and active surveillance [10]. However, no direct comparison to patients without RTR was performed. The inclusion of multiple treatment modalities [8] and the relatively low number of patients treated with a single management strategy may have hampered interpretation of the results. An analysis of surgical outcomes in a multicenter contemporary French cohort involved comparison with a no-RTR group, but the RTR group was relatively small and no standardized statistical methodology was used for comparison of the results [15].

Our aim here was to assess RP results in an RTR group and to compare these with results for a no-RTR group from a large multi-institutional cohort.

2. Patients and methods

2.1. Data source and study population

We identified all patients aged ≥18 yr undergoing RP for cN0M0 PCa and with a history of RTR at seven European tertiary referral centers between 2001 and 2022, leading to an RTR group of 102 patients. A multi-institutional cohort of patients with cN0M0 PCa treated with RP between 2004 and 2022, which included 2339 patients without RTR, was used for comparison. Exclusion criteria consisted of history of other organ transplant, clinically positive lymph nodes (cN+) and/or metastatic disease (cM+) on conventional imaging (axial abdominal computed tomography and/or multiparametric magnetic resonance imaging and a bone scan when appropriate, in accordance with the European Association of Urology guidelines). Two authors (G.M. and A.M.) independently reviewed the quality of the data as previously described [14].

2.2. Outcomes of interest

The primary outcome was comparison of systemic cancer progression between the RTR and no-RTR groups. Secondary outcomes consisted of (1) other oncological outcomes, including biochemical recurrence (BCR), local recurrence, overall mortality (OM), cancer-specific mortality, and other-cause mortality; and (2) perioperative outcomes, including operative time (OT, in minutes), estimated blood loss (EBL, in ml), hospital length of stay (LOS, in days), time to bladder catheter removal (in days), and 30-d postoperative complication rates.

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BCR was defined as rising prostate-specific antigen (PSA) that was undetectable after RP and progressively increased to 0.2 ng/ml. Postoperative complications were graded using the Clavien-Dindo classification, with major complications classed as grade ≥3 [12].

We also evaluated early urinary continence (UC) recovery at 6 mo after surgery. UC recovery was defined as the use of zero or one safety pad/d at the last follow-up visit. UC recovery was assessed at 3, 6, and 12 mo after RP, then every 6 mo for 3 yr, and annually thereafter.

Baseline demographic, perioperative, and postoperative variables were recorded. For the RTR cohort, data for the following characteristics were also collected: age at the start of dialysis, age at RTR, causes of renal failure, type of donor (cadaveric vs living), and classes of immunotherapy (steroids vs mTOR inhibitors vs calcineurin inhibitors vs antiproliferative agents).

2.3. Statistical analysis

All analyses involved comparison of results for the RTR and no-RTR groups. Seven analytical steps were performed. First, 4:1 propensity score matching (PSM) between RTR and no-RTR patients was conducted to reduce potential differences between the cohorts. Matching variables consisted of age at RP, PSA, International Society of Urological Pathology (ISUP) grade group at final pathology, and pT and pN stages.

Second, Kaplan-Meier plots were generated for rates of BCR, local recurrence, systemic progression, and OM, stratified by RTR status. Third, the association between RTR status and BCR was tested in multivariable Cox regression models. Adjustment variables consisted of ISUP grade group at final pathology, pT stage, pN stage, and surgical margin status. The relatively low number of events regarding the other oncological outcomes (local recurrence, systemic progression, and OM) precluded further meaningful multivariable analyses.

Fourth, we conducted multivariable Poisson log-linear regression analyses to test the association of RTR status with OT, EBL, LOS, and time to bladder catheter removal. Covariates consisted of age at RP, body mass index (BMI), smoking habit, diabetes, American Society of Anesthesiologists (ASA) score, cT stage, surgical approach, lymph node dissection (LND), and nerve-sparing (NS) technique.

Fifth, we performed multivariable logistic regression analyses to test the association of RTR status with 30-d postoperative complications. Covariates consisted of age at RP, BMI, diabetes, ASA score, surgical approach, and LND.

Sixth, we carried out multivariable logistic regression analyses to test the association of RTR status with UC recovery at 6 mo after RP. Covariates consisted of age at RP, BMI, cT stage, NS technique, and additional treatments.

Finally, the multivariable analyses for perioperative and functional outcomes were repeated in sensitivity analyses for the RTR cohort alone. Covariates consisted of the time between RTR and RP, age at RP, number of immunosuppression agents, and surgical approach.

R v4.1.2 (R Foundation for Statistical Computing, Vienna, Austria) was used for all analyses. All tests were two-sided, with the level of significance set at $p < 0.05$.

3. Results

3.1. Baseline characteristics

Table 1 lists baseline characteristics for the two cohorts before and after 4:1 PSM. The RTR group had greater BMI and a higher rate of ASA scores of 3–4, and lower rates of minimally invasive RP, LND, and bilateral NS (all $p < 0.05$; Table 1). The RTR group also had significantly less aggressive PCa according to pT stage at final pathology ($p = 0.034$).

After PSM, no major differences persisted between the groups except for ASA score, which was higher in the RTR group (ASA score 3–4: 46% vs 6% for), and rates of minimally invasive RP and bilateral NS, which were higher in the no-RTR group (100% vs 38%, and 82% vs 12%, respectively; all $p < 0.001$). After RP, rates of adjuvant radiotherapy (12% vs 6%; $p = 0.002$) and androgen deprivation therapy (11% vs 3%; p = 0.05) were higher in the RTR group (Table 1).

Additional characteristics of the RTR cohort are listed in Supplementary Table 1. The median time from RTR to RP was 118 mo (IQR 63–186). The most frequent cause of renal failure was chronic glomerulonephritis (35%) and 86% of the transplants were from a cadaveric donor. Some 83% of the RTR patients were taking calcineurin inhibitors at the time of RP.

3.2. Oncological outcomes

Figure 1 shows Kaplan-Meier plots for oncological outcomes at 36 mo. The median follow-up 42 mo for the RTR cohort and 40 mo for the no-RTR cohort. After PSM, the OM rate was higher in the RTR group (17% vs 0.5%; $p < 0.001$). No PCa-specific deaths occurred in either cohort (all deaths were related to other causes) and there were no differences in the rates of local recurrence (2% vs 1%; $p = 0.3$), systemic progression (2% vs 0%; $p = 0.1$), or BCR (11% vs 11%; $p = 0.9$).

Multivariable Cox analyses (Table 2) revealed that ISUP grade at final pathology, positive surgical margin status, and pT stage ≥3 (all $p < 0.05$) but not RTR status (hazard ratio 0.76, 95% confidence interval [CI] 0.38–1.52; $p = 0.4$) were independently associated with BCR. Owing to the low number of events (Fig. 1), no multivariable analyses for local or systemic recurrence or progression were possible.

3.3. Perioperative and functional outcomes

EBL, LOS, time to catheter removal, and rates of postoperative overall and major complications were higher in the RTR cohort (all $p < 0.001$; Table 3); OT did not differ significantly between the groups ($p = 0.09$). A detailed list of complications is provided in Supplementary Table 2. No cases of graft rejection and one case of ureteral injury were observed during RP in the RTR group. The UC recovery rate at 6 mo was 75% in the RTR group and 89% in the no-RTR group ($p < 0.001$; Table 3).

Multivariable analyses revealed that RTR was independently associated with longer OT, LOS, and time to bladder catheter removal and higher EBL, but not with the rates of 30-d postoperative complications and UC recovery at 6 mo after RP (Fig. 2).

3.4. RTR sensitivity analyses

Multivariable sensitivity analyses for the RTR cohort alone revealed that age at RP, use of two or more immunosuppressants, and open RP were associated with longer OT and higher EBL; age and use of two or more immunosuppressants were also associated with longer LOS (all $p < 0.001$; Table 4). Open RP was associated with a lower

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Table 1 – Characteristics of patients treated with RP for prostate cancer, stratified by RTR status before and after propensity score matching

Parameter	Before propensity score matching				After 4:1 propensity score matching [a]			
	Overall (n = 2441)	No RTR (n = 2339)	RTR (n = 102)	p value [b]	Overall (n = 510)	No RTR (n = 408)	RTR (n = 102)	p value [b]
Median age at RP, yr (IQR)	64 (58–68)	64 (58–68)	62 (58–68)	0.3	63 (57–69)	63 (57–69)	62 (58–68)	0.8
Median BMI, kg/m^2 (IQR)	25.3 (23.7–27.3)	25.3 (23.7–27.2)	26.0 (24.0–28.6)	0.035	25.4 (23.7–27.7)	25.3 (23.6–27.4)	26.0 (24.0–28.6)	0.2
Median PSA at PBx, ng/ml (IQR)	6.0 (4.7–8.5)	6.0 (4.7–8.6)	6.2 (5.1–7.8)	0.9	5.9 (4.5–8.1)	5.8 (4.4–7.9)	6.2 (5.1–7.8)	0.8
cT stage, n (%)				0.1				0.09
cT1–2	2293 (94)	2202 (94)	91 (89)		490 (96)	399 (98)	91 (89)	
cT3–4	148 (6)	137 (6)	11 (11)		20 (4)	9 (2)	11 (11)	
ISUP grade at PBx, n (%)				0.9				0.1
1–3	2172 (89)	2082 (89)	90 (89)		466 (93)	377 (94)	90 (89)	
4–5	269 (11)	257 (11)	12 (11)		35 (7)	24 (6)	12 (11)	
D'Amico high-risk group, n (%)	404 (17)	386 (17)	18 (18)	0.6			18 (18)	0.3
ASA score, n (%)				<0.001				<0.001
1–2	2215 (91)	2160 (92)	55 (54)		440 (86)	385 (94)	55 (54)	
3–4	226 (9)	179 (8)	47 (46)		70 (14)	23 (6)	47 (46)	
RP approach, n (%)				<0.001				<0.001
Open	63 (2.6)	0 (0)	63 (62)		63 (12)	0 (0)	63 (62)	
Minimally invasive	2378 (97)	2339 (100)	39 (38)		447 (88)	408 (100)	39 (38)	
Lymph node dissection, n (%)	1711 (70)	1683 (72)	28 (27)	<0.001	145 (28)	117 (29)	28 (27)	0.8
Nerve-sparing surgery, n (%)				<0.001				<0.001
Monolateral	249 (10)	237 (10)	12 (12)		48 (9)	36 (9)	19 (19)	
Bilateral	1803 (74)	1784 (76)	19 (19)		353 (69)	334 (82)	12 (12)	
Pathological ISUP grade, n (%)				0.6				0.8
1–3	2,081 (85)	1992 (85)	89 (87)		449 (88)	360 (88)	89 (87)	
4–5	360 (15)	347 (15)	13 (13)		61 (12)	48 (12)	13 (13)	
pT stage, n (%)				0.034				0.6
pT2	1475 (60)	1403 (60)	72 (71)		372 (73)	300 (74)	72 (71)	
pT3a	745 (31)	718 (31)	27 (26)		128 (25)	101 (25)	27 (26)	
pT3b-4	221 (9)	218 (9)	3 (3)		10 (2)	7 (2)	3 (3)	
pN stage, n (%)				<0.001				0.5
pN0	1507 (62)	1485 (63)	22 (22)		123 (24)	101 (25)	22 (22)	
pN1	204 (8)	198 (9)	6 (6)		22 (4)	16 (4)	6 (6)	
PLN template, n (%)				NA				NA
Unilateral (CL to graft)	5 (0.3)	0 (0)	5 (18)		5 (3.5)	0 (0)	5 (18)	
Bilateral	1706 (99.7)	1683 (100)	23 (82)		140 (96.5)	117 (100)	23 (82)	
Positive surgical margin, n (%)	527 (22)	504 (22)	23 (23)	0.8	112 (22)	89 (22)	23 (23)	0.2
Additional radiotherapy, n (%)				0.008				0.002
Adjuvant radiotherapy	195 (8)	183 (8)	12 (12)		36 (7)	24 (6)	12 (12)	
Salvage radiotherapy	177 (7)	177 (8)	0 (0)		16 (3)	16 (4)	0 (0)	
ADT, n (%)	124 (5)	113 (5)	11 (11)	0.007	23 (5)	12 (3)	11 (11)	0.

RTR = renal transplant receipt; PSA = prostate-specific antigen; ISUP = International Society of Urological Pathology; ASA = American Society of Anesthesiologists; NA = not applicable; RP = radical prostatectomy; IQR = interquartile range; BMI = body mass index; PBx = prostate biopsy; CL = contralateral; PLN = pelvic lymph node; ADT = androgen deprivation therapy.

[a] Variables used for matching were age at RP, PSA, ISUP grade group at final pathology, and pT and pN stages.

[b] Wilcoxon rank-sum test, Pearson's χ^2 test, or Fisher's exact test.

likelihood of UC recovery at 6 mo (odds ratio 0.15, 95% CI 0.10–0.46, p = 0.022); no other factors were significantly associated with UC recovery (Table 4).

4. Discussion

We report RP outcomes for the largest series of RTR patients. To the best of our knowledge, this is also the first comparison with a no-RTR cohort using matched paired analysis within the context of a non–registry-based study to reduce potential biases. Several findings are of interest.

First, oncological RP outcomes were comparable for the RTR and no-RTR groups. At medium-term follow-up, there were no differences in the rates of systemic progression and BCR. These results were confirmed by multivariable analyses. Furthermore, the rate of adverse oncological outcomes in the RTR group were relatively low and similar to previous reports [3,11], including findings for a multicenter cohort [15]. No PCa deaths occurred.

Interestingly, many baseline PCa characteristics in the RTR group were comparable to those in the no-RTR group even before matching, except pT and pN stages in the no-RTR group. These findings provide an indirect contrast to the sole report of higher rates of locally advanced disease in the RTR setting [16].

Second, the overall mortality rate was higher in the RTR group than in the no-RTR group (17% vs <1%). This is in sharp contrast to the absence of PCa-related deaths in the RTR group, mirroring the non-RTR group, and the low rates recently reported for the ProtecT trial [9]. When localized,

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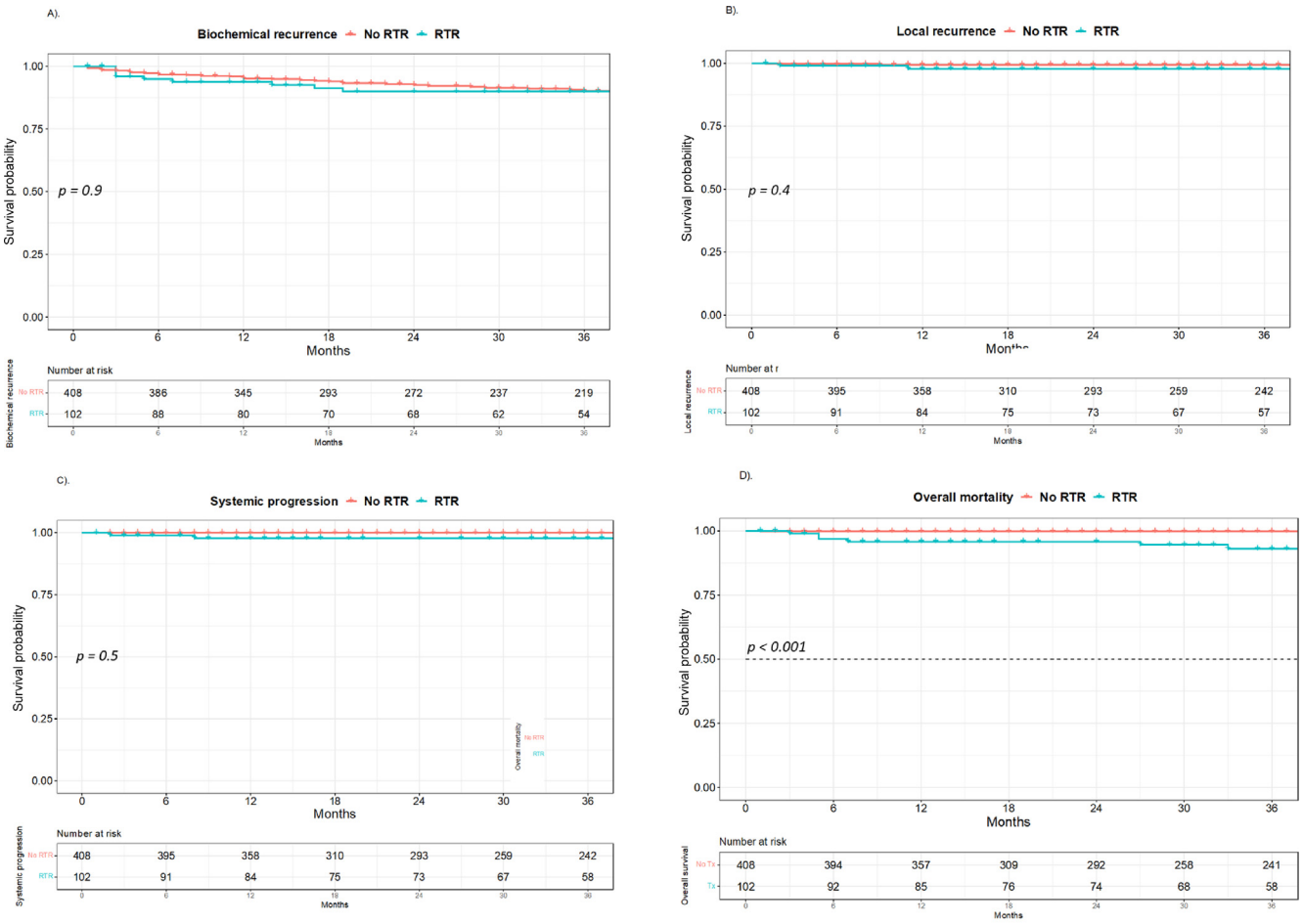

Characteristic	Overall, *n* = 408	No RTR, *n* = 306	RTR, *n* = 102	*p* value
Median FU, mo (IQR)	40 (19, 72)	40 (20, 72)	42 (19, 75)	0.8
Biochemical recurrence, n (%)	56 (11%)	45 (11%)	11 (11%)	0.9
Local recurrence, n (%)	6 (1.2%)	4 (1.0%)	2 (2.0%)	0.3
Systemic progression, n (%)	2 (0.4%)	0 (0%)	2 (2.0%)	0.1
Other-cause mortality, n (%)	19 (3.7%)	2 (0.5%)	17 (17%)	**<0.001**
Overall mortality, n (%)	19 (3.7%)	2 (0.5%)	17 (17%)	**<0.001**

Fig. 1 – Kaplan-Meier curves for (A) biochemical recurrence, (B) local recurrence, (C) systemic progression, and (D) overall survival for patients treated with radical prostatectomy for prostate cancer, stratified by renal transplant receipt (RTR) status. FU = follow-up; IQR - interquartile range.

Table 2 – Multivariable Cox regression for independent predictors of biochemical recurrence of prostate cancer

Factor	HR (95% CI)	*p* value
Renal transplant receipt	0.76 (0.38–1.52)	0.4
ISUP grade 4–5 at pathology	2.22 (1.12–4.41)	0.022
≥pT3 stage	4.36 (2.32–8.18)	<0.001
pN1 stage	1.77 (0.80–3.91)	0.2
Positive surgical margin	1.99 (1.11–3.60)	0.024

HR = hazard ratio; CI = confidence interval; ISUP = International Society of Urological Pathology.

PCa is not a major driver of mortality in the RTR population and has only a marginal influence on survival. Despite important advances in RTR care, morbidity rather than PCa influences life expectancy in this population. In the current RTR cohort, almost all patients had previously undergone dialysis, almost one in four had diabetes, and almost one in five had secondary malignancies. All these factors are well-known independent predictors of worse survival. While our finding is in line with the survival reported for RTR [17], it is from the largest series of RTR patients with a subsequent PCa diagnosis.

Third, RP seems to be feasible in the RTR setting without compromising the graft. While multivariable analyses revealed no differences in the rates of complications and UC recovery, these were higher in the RTR group on univariate comparison and must be taken into account because of

Table 3 – Surgical outcomes of radical prostatectomy for prostate cancer according to RTR status

Parameter	Overall (n = 510)	No RTR (n = 408)	RTR (n = 102)	p value [a]
Median operative time, min (IQR)	200 (160–240)	197 (158–240)	210 (172–252)	0.09
Medial EBL, ml (IQR)	200 (150–350)	200 (150–350)	400 (250–800)	<0.001
Hospital stay, d (IQR)	4.0 (3.0–6.0)	3.5 (3.0–6.0)	6.0 (4.0–9.0)	<0.001
Time to bladder catheter removal, d (IQR)	7.0 (5.0–10.0)	5.0 (5.0–7.0)	11.0 (8.0–16.0)	<0.001
30-d POPCs, n (%)	77 (15)	49 (12)	28 (27)	<0.001
30-d Clavien grade ≥3 POPCs, n (%)	23 (5)	11 (3)	12 (12)	<0.001
6-mo urinary continence recovery, n (%)	440 (86)	363 (89)	77 (75)	<0.001

IQR = interquartile range; RTR = renal transplant receipt; EBL = estimated blood loss; POPCs = postoperative complications.
[a] Wilcoxon rank-sum test, Pearson's χ^2 test, or Fisher's exact test.

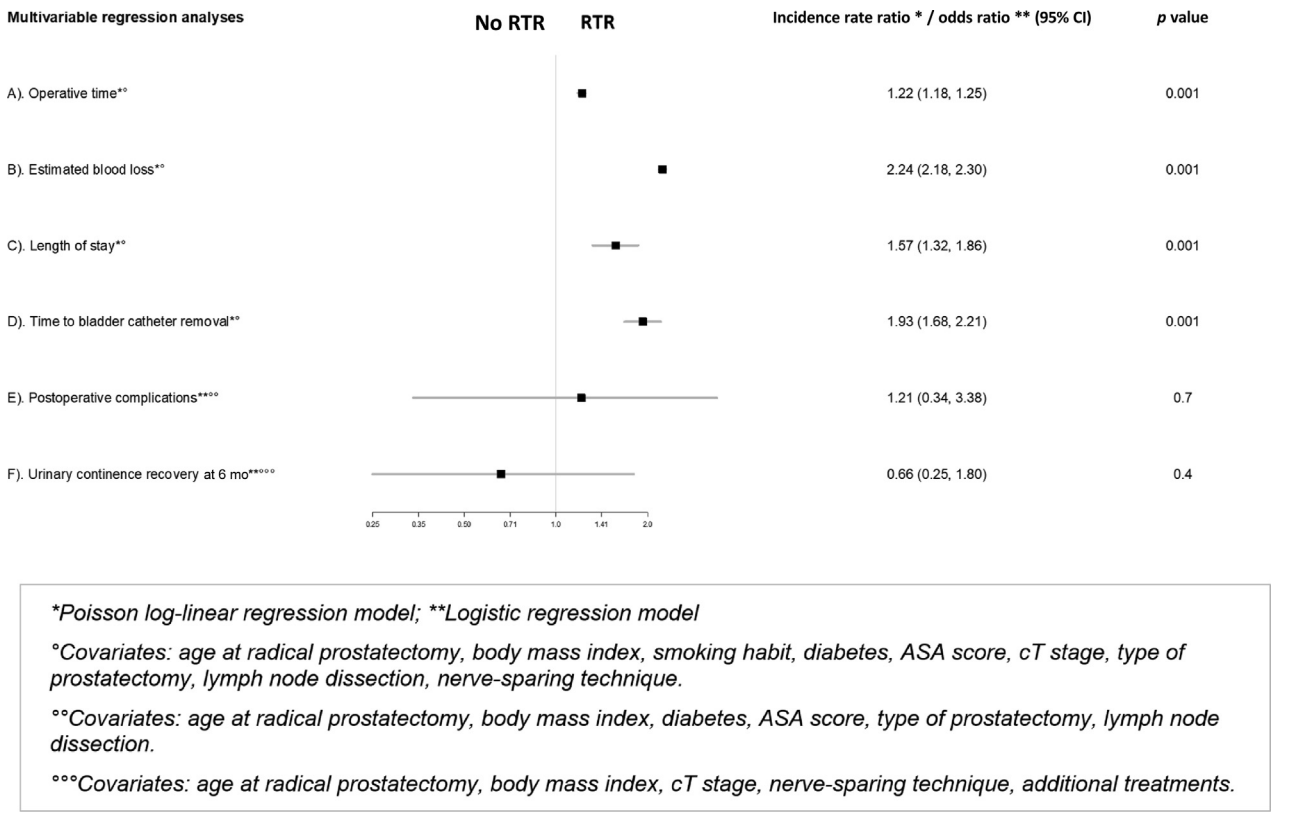

Fig. 2 – Multivariable Poisson log-linear regression and logistic regression analyses testing the association between renal transplant receipt (RTR) and surgical and functional outcomes: (A) operative time; (B) estimated blood loss; (C) length of stay; (D) time to bladder catheter removal; (E) 30-d postoperative complications; and (F) urinary continence recovery at 6 mo. ASA = American Society of Anesthesiologists; CI = confidence interval.

the study limitations. OT, EBL, LOS, and catheterization time were all greater in the RTR group. The results probably reflect the greater frailty of these patients and the higher surgical complexity owing to the presence of the graft in the iliac fossa. The longer catheterization time may be related to caution regarding potential damage to the graft due to anastomotic complications, although this factor may also be influenced by the different learning curves for RP in the two groups. Interestingly, the UC recovery rate was significantly higher for the no-RTR group after matching, but this difference was no longer significant after multivariable adjustments for factors including NS, which is widely associated with UC preservation [18]. UC recovery certainly depends on good preservation of the bladder neck and urethral sphincter, which can sometimes be challenging in the RTR setting because of the reduced operative field and adhesions, if present. The reason for the lower NS rate for the RTR group remains unclear. A historical fear of greater PCa aggressiveness due to immunosuppression, poor baseline erectile function among RTR patients, frequently related to previous dialysis, and the lower number of robotic procedures may be among possible reasons for the lower NS rate.

Fourth, we investigated possible factors associated with PCa outcomes in RTR. As detailed for a previous study that included multiple treatment modalities [8], no RTR-related

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Table 4 – Sensitivity multivariable Poisson log-linear regression and logistic regression analyses for 102 patients treated with RP for prostate cancer after RTR

Parameter	Poisson log-linear regression						Logistic regression			
	Operative time		Estimated blood loss		Length of stay		POPCs		UC recovery at 6 mo	
	IRR (95% CI)	*p* value	IRR (95% CI)	*p* value	IRR (95% CI)	*p* value	OR (95% CI)	*p* value	OR (95% CI)	*p* value
Time from RTR to RP	1.00 (0.99–1.00)	0.1	0.99 (0.99–1.00)	0.2	1.00 (1.00–1.01)	0.4	0.99 (0.99–1.00)	0.2	0.99 (0.99–1.01)	0.6
Age at RP	1.01 (1.01–1.03)	<0.001	1.02 (1.01–1.02)	<0.001	1.03 (1.01–1.04)	<0.001	1.04 (0.95–1.14)	0.5	0.90 (0.80–1.00)	0.057
ISTx with ≥2 agents	1.08 (1.04–1.13)	<0.001	0.58 (0.56–0.60)	<0.001	1.96 (1.53–2.53)	<0.001	3.64 (0.76–7.09)	0.1	0.63 (0.13–2.65)	0.5
Open RP	0.83 (0.80–0.86)	<0.001	0.56 (0.54–0.58)	<0.001	1.01 (0.83–1.24)	0.9	3.31 (0.84–7.03)	0.1	0.15 (0.10–0.46)	0.022

IRR = incidence rate ratio; CI = confidence interval; RP = radical prostatectomy; RTR = renal transplant receipt T_{RTR-RP} = time between RTR and RP; ISTx = immunosuppression therapy; POPCs = postoperative complications; UC = urinary continence; OR = odds ratio.

factors, including causes of renal failure, the immunosuppression regimen, and/or graft-related features, were associated with oncological outcomes. Our findings stand in contrast to univariable analysis results from a smaller retrospective RP cohort regarding a possible increase in the risk of locally advanced and extraprostatic PCa when taking azathioprine together with calcineurin inhibitors. Conversely, older age and use of two or more immunosuppressants were related to longer OT and LOS and greater EBL, and should be kept in mind when deciding on the indication for surgery in this population. Finally, open surgery was associated with longer OT and greater EBL and to some extent with worse UC recovery. While the robotic RP approach is gaining ground in the RTR setting, our findings require further investigation because of the study limitations and the well-established noninferiority of open surgery when performed by expert surgeons [19–21].

From a clinical perspective we showed that RTR patients with localized PCa treated with RP are much more likely to die from causes other than from PCa and to have longer OT and LOS. On one hand, we observed excellent oncological and continence outcomes for RP in an RTR cohort, proving its feasibility for this population. On the other hand, our findings question the appropriateness of active treatment for all localized PCa cases, since almost one in five patients died at median follow-up of slightly more than 3 yr, with no deaths being PCa-related. Even though the surgeries were carried out at tertiary referral institutions, LOS and OT were longer for the RTR group, which can probably be attributed to frailty related to concomitant comorbidities and graft management, while yielding unclear overall and PCa-related survival benefits.

From a research perspective, our aim was to highlight some baseline and PCa features that may influence disease and surgical outcomes, but no major predictors were identified apart from age and the number of immunosuppressant agents for complication rates and operative time. To reduce overtreatment, research should focus on patient selection and personalized management to define cutoffs for selection of men who are likely to benefit from active PCa treatment and possible identification of those at higher risk of complications. There is a need to investigate whether other treatment modalities may be less morbid than surgery and thus more appropriate for PCa management in the RTR population.

Limitations of our study need to be kept in mind. The retrospective nature of the study probably hampered data quality. Despite being the largest RP series in RTR to date, the number of patients may be not appropriate to identify all factors with a possible influence on outcomes via multivariable analyses. Although the noninferiority of open over minimally invasive surgery has been well demonstrated in the standard setting without RTR [19–21], the fact that the majority of RP procedures in the RTR cohort involved an open approach, in contrast to none in the no-RTR cohort, represents a potential unmodifiable source of bias. This being acknowledged, our study provides novel findings on an uncharted topic and a highly generalizable picture of PCa management in RTR, with reasonable uncertainty margins. Finally, sirolimus, despite being used in only a minority of RTR patients, may have altered PSA values. However, this would have involved a decrease in PSA, further confirming the absence of greater risk in the RTR compared to the no-RTR group.

As previously discussed by our group and others [3,8,11], efforts are required to overcome current limitations via multicenter prospective international registries to improve the management of PCa for RTR patients.

5. Conclusions

Oncological and continence outcomes after RP for localized PCa were comparable between the RTR and no-RTR groups. However, the risk of death from other causes was significantly higher in the RTR group, highlighting a need for more careful selection of RTR patients for RP to reduce overtreatment and related side effects. Prospective multicenter evidence is urgently needed to validate our findings.

***Author contributions*:** Giancarlo Marra had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Marra, Tappero, Marquis, Gontero.
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Analysis and interpretation of data: Marra, Tappero, Barletta, Marquis, Gontero.
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Critical revision of the manuscript for important intellectual content: All authors.
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Appendix B. Supplementary data

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