International Urology and Nephrology (2023) 55:2439–2445
https://doi.org/10.1007/s11255-023-03709-8

UROLOGY - ORIGINAL PAPER

Does renal failure worsen radiation cystitis following radical prostatectomy?

Ricky Chen[1] · Sikai Song[1] · Akin S. Amasyali[1] · Rose Leu[1] · Kanha Shete[1] · Cayde Ritchie[1] · Matthew Buell[1] · Catalina Baas[1] · Joshua D. Belle[1] · Daniel Jhang[1] · Ala'a Farkouh[1] · D. Duane Baldwin[1]

Received: 9 June 2023 / Accepted: 8 July 2023 / Published online: 13 July 2023

Abstract

Objective To investigate the impact of renal function on the risk, severity, and management of radiation cystitis in patients who underwent postoperative radiation therapy for prostate cancer.

Methods Retrospective data was assessed from patients treated with adjuvant/salvage radiation therapy at a single academic institution between 2006 and 2020. The incidence, severity, and management of radiation cystitis were compared between three groups: CKD 0–2, CKD 3–4, and CKD 5. Associations of clinicopathologic factors with radiation cystitis were assessed in univariate and multivariate Cox regression models.

Results A total of 110 patients who underwent radiation therapy following robot-assisted laparoscopic radical prostatectomy were included. The incidence of radiation cystitis following postoperative radiation therapy was 17% with a median presentation time of 34 months (interquartile range 16–65 months). The incidence of radiation cystitis was 100% in CKD 5 patients compared to 15% in CKD 0–2 and 17% in CKD 3–4 patients ($p < 0.001$). CKD 5 patients required more treatments, emergency department visits, and longer hospitalization times than CKD 0–4 patients (all $p < 0.001$). Multivariate analyses identified CKD 5 as the only significant factor associated with radiation cystitis (HR = 10.39, $p = 0.026$).

Conclusion End-stage renal failure is associated with the risk and severity of radiation cystitis in patients receiving postoperative radiation therapy. Knowledge of the potential morbidity of this complication in this population could guide physicians and patients as they evaluate risks and benefits prior to selecting adjuvant or salvage radiation therapy.

Keywords Cystitis · Hematuria · Radiotherapy · Prostate cancer · Kidney failure · Chronic · Prostatectomy

Introduction

Current transplantation guidelines recommend that end-stage renal disease (ESRD) patients with aggressive prostate cancer receive definitive treatment prior to renal transplantation [1, 2]. Post-transplant immunosuppression may act as a double-edged sword by increasing both graft survival and risk of metastatic progression. Patients most frequently undergo definitive treatment by either radical prostatectomy or radiation therapy (RT). Following robot-assisted laparoscopic radical prostatectomy (RALP), some patients also receive RT as either an adjuvant regimen for adverse pathology or salvage treatment for biochemical recurrence [3]. However, RT can lead to adverse effects, including radiation cystitis (RC).

RC is a severe adverse effect of RT that may lead to life-threatening hemorrhage. The incidence of RC is 5–16.2% with a mean delay in presentation of 2–3 years [4–8]. Management of RC may be challenging, often requiring emergency department (ED) visits, hospitalizations, and interventions including catheterization, bladder irrigation, blood transfusion, intravesical treatment, hyperbaric oxygen (HBO), and operative treatment [9].

Patients with ESRD who receive postoperative RT for prostate cancer may be at higher risk for developing RC. Although the etiology is not definitively known, lower bladder volumes in ESRD and a new bladder position after prostatectomy could result in higher radiation doses to the bladder [7, 10–12]. There is currently no literature reporting the impact of renal failure on RC following postoperative RT for

✉ D. Duane Baldwin
dbaldwin@llu.edu

[1] Department of Urology, Loma Linda University Health, 11234 Anderson Street, Room A560, Loma Linda, CA 92354, USA

prostate cancer. The purpose of this study is to investigate the relationship between renal function on the risk, severity, and management of RC in patients with prostate cancer who have undergone postoperative RT.

Methods

After institutional review board approval (IRB# 5220295), a retrospective review identified 1271 patients who underwent RALP between 2006 and 2020 at a single academic institution. Of these, 110 patients received either adjuvant or salvage RT. Patients with primary RT for prostate cancer, pelvic radiation for other etiologies, or a history of bladder cancer were excluded. RC was diagnosed by the occurrence of gross hematuria without other explainable causes such as infection, genitourinary cancer, or drug-induced cystitis. The severity of RC was classified using the Common Terminology Criteria for Adverse Events (CTCAE) version 5.0 grading system [7–10]. Severe RC was defined as grade 3 or higher.

Patients were divided into three groups based on renal function: CKD 0–2, 3–4, and 5. The demographics, clinical characteristics, and management of RC were analyzed and compared. Clinical data recorded included antithrombotic (antiplatelet/anticoagulant) therapy, prostate-specific antigen (PSA) levels, pathological stage, Gleason score, time interval from RALP to the start of RT, radiation modality, total radiation dose, and length of follow-up. Hematuria treatments included catheterization, hand irrigation, continuous bladder irrigation (CBI), intravesical agents, blood transfusion, HBO, and operative intervention. The number of ED visits, hospital admissions, and hospital lengths of stay were also compared.

Statistical analysis included ANOVA and Chi-square to compare outcomes between CKD groups. Associations of clinicopathologic factors with RC were assessed in univariate and multivariate Cox regression models. Kaplan–Meier analysis estimated the cumulative incidence of RC by CKD stage. Statistical computations were conducted using IBM SPSS Statistics v.24.0 (IBM Corp., Armonk, NY). Significance was defined as a p value of < 0.05.

Results

Patient demographics and characteristics

One hundred and ten patients received adjuvant/salvage RT following RALP (Table 1). Among these, 101 had CKD 0–2, 7 had CKD 3–4, and 2 had CKD 5. The average age in years and BMI at the first RT session were 67.4 and 29, respectively. The mean pre-RALP PSA level was 12.5 ng/mL, the mean pre-RT PSA level was 0.462 ng/mL, and the mean post-RT PSA level was 0.039 ng/mL at 3–6 months of follow-up. The proportion of patients with undetectable PSAs at 3–6 months following RT was 73%. The mean time interval from RALP to the start of RT was 17.7 and was significantly less in CKD 0–2 patients compared to CKD 3–4 and 5 patients ($p = 0.029$, Table 1). The most common pathologic cancer stage was T3b in 40% of patients, followed by T3a (32%). The most common Gleason score was 3 + 4 in 58% of patients followed by Gleason 4 + 4. The median length of follow-up after RT was 34 months. Most patients were not prescribed antithrombotic therapy (59.1%); however, all CKD 5 patients were receiving antithrombotic therapy ($p = 0.086$). There were no significant differences in other demographic and clinical variables among the CKD 0–2, 3–4, and 5 groups ($p > 0.05$, Table 1).

Radiation therapy modality

Of the 92 patients with available treatment modality data, 55% received proton therapy, 33% received intensity-modulated radiation therapy (IMRT), 11% received external beam radiation therapy (EBRT), and 1% received a combination of IMRT and proton therapy (Table 1). The proportion of patients receiving adjuvant and salvage RT was 42% and 58%, respectively. There were no significant differences between radiation modality ($p = 0.677$) and adjuvant/salvage RT ($p = 0.972$) among CKD patients. The mean total dose of radiation delivered was 68.3 Gy with no significant difference among CKD groups ($p = 0.712$, Table 1).

Incidence of radiation cystitis

Of the 93 patients that had a minimum of 3 months of follow-up, 17% developed RC (Table 2). All CKD 5 patients developed RC compared to 15% of CKD 0–2 and 17% of CKD 3–4 patients ($p < 0.001$). There was no difference in the incidence of RC between the CKD 0–2 and 3–4 patients ($p = 0.928$). All CKD 5 patients developed severe hematuria compared to 1% of CKD 0–2 and 17% of CKD 3–4 patients ($p < 0.001$). CKD 3–4 patients had a higher incidence of severe RC than CKD 0–2 patients ($p = 0.012$). There was no significant difference in the overall incidence of mild RC among CKD patients ($p = 0.523$). The mean time elapsed from the end of RT to the onset of RC was 29.0 months with no significant difference among CKD groups ($p = 0.369$).

Treatment and management of radiation cystitis

All patients with CKD 5 required interventions for RC (catheterization, hand irrigation, and CBI) compared to 1% of those with CKD 0–2 and 17% with CKD 3–4 ($p < 0.001$, Table 2). Similarly, all CKD 5 patients required blood

Table 1 Patient demographics and clinical characteristics

	Total N = 110 Mean (SD)	CKD 0–2 N = 101 Mean (SD)	CKD 3–4 N = 7 Mean (SD)	CKD 5 N = 2 Mean (SD)	*p* value
Age (years)	67.4 (7.7)	67.7 (7.8)	63.3 (6.6)	65.5 (0.7)	0.323
BMI (kg/m^2)	29.0 (4.5)	28.7 (4.4)	31.1 (4.8)	34.9 (4.6)	0.066
Pre-RALP PSA (ng/mL)	12.5 (13.3)	13.1 (13.8)	6.9 (4.7)	4.8 (3.0)	0.358
Pre-RT PSA (ng/mL)	0.462 (2.02)	0.499 (2.13)	0.141 (0.175)	0.070 (0.014)	0.873
Post-RT PSA (ng/mL)	0.039 (0.108)	0.041 (0.112)	0.023 (0.041)	0.02 (0.00)	0.870
Follow-up (months)					0.798
Median (IQR)	34.0 (16.0–65.0)	32.0 (16.0–65.0)	54.0 (25.0–64.3)	28.5 (23.3–33.8)	
Time interval RALP-RT (months)	17.7 (17.3)	16.2 (10.0)	33.4 (31.5)	27.0 (22.6)	**0.029**
Dose (Gy)	68.3 (3.1)	68.3 (3.3)	67.6 (1.8)	69.3 (1.3)	0.769
	N (%)	N (%)	N (%)	N (%)	
pT-stage					0.255
T1	1 (1)	1 (1)	0	0	
T2	32 (30.0)	26 (26.5)	4 (57)	2 (100)	
T3	72 (67.3)	69 (70.4)	3 (43)	0	
T4	2 (1.9)	2 (2.0)	0	0	
Gleason score					0.744
6	3 (2.8)	3 (3.1)	0	0	
7	62 (57.9)	55 (56.1)	5 (71)	2 (100)	
8	23 (21.5)	21 (21.4)	2 (29)	0	
9	19 (17.8)	19 (19.4)	0	0	
RT modality					0.677
Proton	51 (54.8)	46 (54.8)	3 (43)	2 (100)	
EBRT	10 (10.8)	10 (11.9)	0	0	
IMRT	31 (33.3)	27 (32.1)	4 (57)	0	
Proton/IMRT	1 (1.1)	1 (1.2)	0	0	
Adjuvant/salvage RT					0.972
Adjuvant	42 (42)	38 (41.8)	3 (43)	1 (50)	
Salvage	58 (58)	53 (58.2)	4 (44)	1 (50)	
Antiplatelet/anticoagulant					0.086
Yes	38 (40.9)	32 (37.6)	4 (67)	2 (100)	
No	55 (59.1)	53 (62.4)	2 (33)	0	

BMI body mass index, *RT* radiation therapy, *RALP* robot-assisted laparoscopic prostatectomy, *Gy* gray, *N* number of patients, *SD* standard deviation, *IQR* interquartile range

transfusion and HBO compared to 0% of CKD 0–2 and 17% of CKD 3–4 patients ($p < 0.001$). CKD 5 patients received 4 compared to 1.2 units of blood for CKD 3–4 patients ($p < 0.001$). CKD 5 patients received 14 compared to 6.7 sessions of HBO for CKD 3–4 patients ($p < 0.001$). CKD 0–2 patients did not require either blood transfusion or HBO.

For operative treatment, 50% of CKD 5 patients received clot evacuation and fulguration compared to 17% of CKD 3–4 patients and 1% of CKD 0–2 patients ($p < 0.001$). CKD 3–4 patients required more interventions (catheterization, hand irrigation, CBI, blood transfusion, and operative treatment), units of blood, and sessions of HBO compared to CKD 0–2 patients (all $p < 0.01$, Table 2). Patients with CKD 5 had more ED visits (3.5 vs 1.0 vs 0.1), more hospitalizations (2.5 vs 1.0 vs 0.1), and longer lengths of stay (12.5 vs 4.0 vs 0.1 days) as compared to CKD 3–4 and CKD 0–2 patients, respectively (all $p < 0.01$, Table 2).

Risk factors for radiation cystitis

Univariate analysis showed that CKD stage was significantly associated with the development of RC (Table 3). Time interval between RALP and RT, antithrombotic therapy, adjuvant/salvage RT, radiation modality, and radiation dose were not associated with RC. Multivariate analysis identified CKD stage as the only significant factor associated with RC

Table 2 Incidence, severity, and treatments of radiation cystitis

	Total N = 93 N (%)	CKD 0–2 N = 85 N (%)	CKD 3–4 N = 6 N (%)	CKD 5 N = 2 N (%)	*p* value
RC	16 (17)	13 (15)	1 (17)	2 (100)	0.007
< grade 3	12 (13)	12 (14)	0	0	0.523
≥ grade 3	4 (4)	1 (1)	1 (17)	2 (100)	< 0.001
Treatment					
Catheterization	4 (4)	1 (1)	1 (17)	2 (100)	< 0.001
Hand Irrigation	4 (4)	1 (1)	1 (17)	2 (100)	< 0.001
CBI	4 (4)	1 (1)	1 (17)	2 (100)	< 0.001
Intravesical Tx	1 (1)	0	1 (17)	0	–
Blood transfusion	3 (3)	0	1 (17)	2 (100)	< 0.001
HBO	3 (3)	0	1 (17)	2 (100)	< 0.001
Operative Tx	3 (3)	1 (1)	1 (17)	1 (50)	< 0.001
	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	*p* value
Blood transfusion (units)	0.16 (0.94)	0	1.2 (2.9)	4 (1.4)	< 0.001
HBO (# sessions)	0.73 (4.87)	0	6.7 (16.3)	14.0 (15.6)	< 0.001
ED visits (#)	0.20 (0.89)	0.1 (0.4)	1.0 (2.4)	3.5 (2.1)	< 0.001
Hospitalizations (#)	0.12 (0.73)	0.01 (0.1)	1.0 (2.5)	2.5 (0.7)	< 0.001
Cumulative hospital stay (days)	0.6 (3.2)	0.1 (0.8)	4.0 (9.8)	12.5 (9.2)	< 0.001
Interval RT-RC (months)	29.0 (22.2)	32.8 (22.9)	6 (0)	16 (5.7)	0.369

RC radiation cystitis, *CBI* continuous bladder irrigation, *HBO* hyperbaric oxygen therapy, *RT* radiation therapy, *ED* emergency department, *SD* standard deviation

Table 3 Univariate and multivariate Cox proportional hazards regression analyses of the association of clinicopathologic variables with radiation cystitis

Variables	Univariate			Multivariate		
	HR	95% CI	*p* value	HR	95% CI	*p* value
Age	0.97	0.91–1.04	0.436			
BMI	1.01	0.89–1.13	0.932			
Gleason Score	0.85	0.46–1.60	0.621			
Pathologic T stage	0.74	0.29–1.91	0.532			
Postoperative RT						
Salvage	Reference					
Adjuvant	0.66	0.23–1.89	0.437			
Interval RALP-RT	1.00	0.97–1.02	0.770	0.98	0.93–1.03	0.405
Anticoagulant/antiplatelet	1.83	0.68–4.92	0.231	1.89	0.47–7.62	0.371
Radiation modality						
Proton	Reference			Reference		
IMRT	0.69	0.22–2.17	0.524	1.00	0.24–4.13	0.995
EBRT	0.37	0.05–2.84	0.336	–	–	–
Radiation dose						
< 70 Gy	Reference			Reference		
≥ 70 Gy	1.60	0.48–5.27	0.443	2.37	0.62–9.09	0.209
CKD group						
0–2	Reference			Reference		
3–4	1.13	0.15–8.68	0.904	1.15	0.11–12.27	0.907
5	**21.27**	**4.16–108.79**	**< 0.001**	**10.39**	**1.33–81.08**	**0.026**

HR hazard ratio, *BMI* body mass index, *RT* radiation therapy, *RALP* robot-assisted laparoscopic prostatectomy, *IMRT* intensity modulated radiation therapy, *EBRT* external beam radiation therapy, *CKD* chronic kidney disease, *Gy* gray, *CI* confidence interval

(hazard ratio: 10.39, p = 0.026). Figure 1 demonstrates the cumulative incidence of RC in the setting of the CKD stage.

Discussion

In this retrospective cohort analysis over a 15-year period, we analyzed 110 prostate cancer patients who received adjuvant/salvage RT. In our study, the incidence of RC was 17% after a median follow-up of 34 months, which is slightly higher than the 5–16.2% reported in previous literature [4–8]. However, all CKD 5 patients in our series developed RC. In contrast, the incidence in patients with CKD 0–2 and 3–4 was 15% (13/85) and 17% (1/6), respectively. Patients with CKD 5 also had a higher incidence of severe RC. Specifically, all CKD 5 patients developed severe RC compared to 17% (1/6) of CKD 3–4 patients and 1% (1/85) of CKD 0–2 patients. When compared to patients with CKD 0–2, those with CKD 3–4 also had a higher incidence of severe RC. To our knowledge, this is the first study to investigate the impact of renal function on RC in the setting of postoperative RT.

The average time to development of RC in our study was 29.0 ± 22.2 months after radiation. This is earlier than the mean time reported in previous series, which ranged from 43.9 to 79.1 months [4, 5]. However, these previous studies included both primary and postoperative RT, while our study only included postoperative RT.

Univariate and multivariate analysis revealed that CKD 5 was the only factor associated with the development of RC (hazard ratio 10.39, p = 0.026). Antithrombotic therapy was not associated with RC. Similarly, Makino et al. reported no association between antithrombotic therapy and RC in a series of patients receiving external beam RT (EBRT) [7]. Sanguedolce et al. found that antithrombotic therapy was associated with an increased risk of hospitalization, but their study did not assess the risk of RC [4].

Multivariate analysis in a recent retrospective study found that postoperative RT had a higher risk of RC compared to primary RT. That study also found that the incidence of radiation proctitis did not differ between primary and adjuvant/salvage RT [7]. These findings suggest that adjuvant/salvage radiation may carry a higher risk of genitourinary toxicity. One possible explanation could be that during RALP, the anterior surface and dome of the bladder are extensively mobilized and pulled down into the pelvis for urethral anastomosis [12]. This surgical mobilization and new position in the pelvis may increase radiation exposure to the bladder which in turn may account for the higher incidence of RC of 17% in our study compared to the 5–16.2% in the literature [4–8]. Subsequent alterations in bladder blood flow [13] after surgery may increase tissue radiation susceptibility. In contrast, the rectum retains its identical anatomic location and blood supply and therefore does not demonstrate any difference in rectal complications following primary or postoperative RT [7].

Bladder volume during RT for prostate cancer has been found to be inversely correlated with the mean radiation dose to the bladder [11] and genitourinary toxicity [10, 14]. Pinkawa et al. discovered that a bladder volume < 180 cc resulted in increased urinary and bowel toxicities [14]. Similarly, Grün et al. found that median bladder volumes < 180 cc also increased the risk of bowel and urinary toxicities ≥ grade 2 by 175% [10]. Therefore, patients with renal dysfunction causing oliguria or anuria

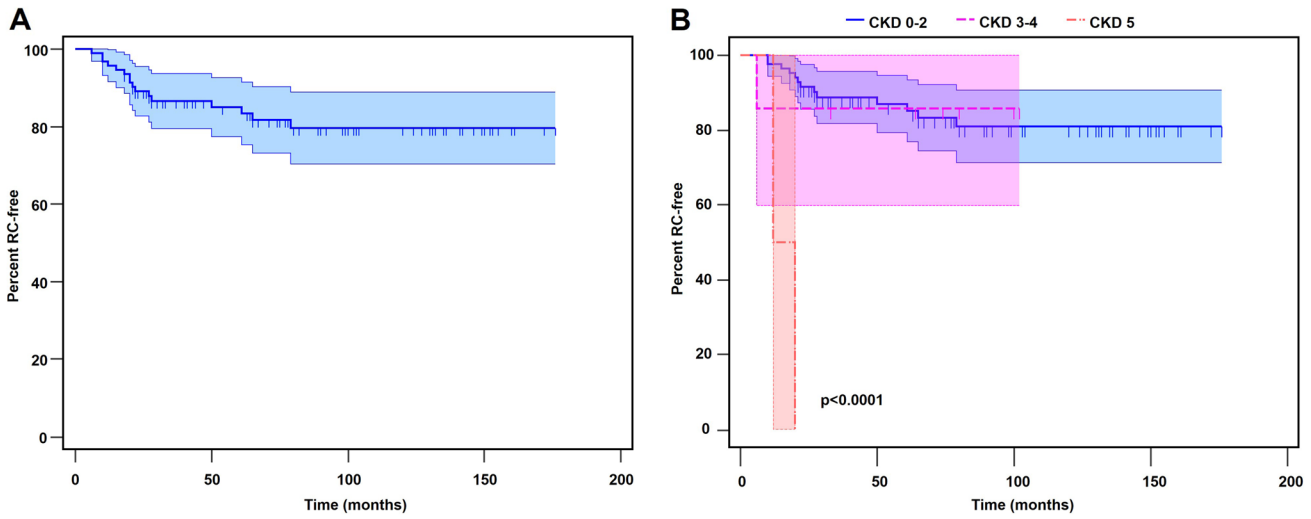

Fig. 1 Kaplan–Meier analysis for **A** overall radiation cystitis-free survival and **B** radiation cystitis-free survival stratified by CKD 0–2, CKD 3–4, and CKD 5

may be at increased risk of RC following postoperative RT.

Renal failure-related coagulation disorders may also contribute to the development of RC following postoperative RT. CKD patients are not only more prone to thrombotic events but also demonstrate increased rates of bleeding due to platelet dysfunction [15]. Incidental radiation of the bladder leads to submucosal vascular fibrosis, bladder ischemia, and subsequent neovascularization, which generates vasculature that is prone to bleeding [16]. In the setting of renal failure-related platelet dysfunction, there may be a higher bleeding risk. Hypercoagulability from renal failure could exacerbate bladder ischemia and further promote neovascularization.

Our study found that the incidence of RC was similar among all radiation modalities. This finding is consistent with several retrospective studies that reported no differences in genitourinary toxicity between IMRT, EBRT, and proton therapy [17, 18].

The treatment of RC can be burdensome for patients, as it may involve invasive procedures, multiple ED visits, and prolonged hospitalizations. Our study found that patients with CKD 5 not only had a higher risk and severity of RC but also required significantly more aggressive treatments, ED visits, hospitalizations, and longer hospital stays compared to CKD 0–4 patients (Table 2).

For this reason, the severe morbidity associated with RC in patients with ESRD poses a challenge in the management of postoperative RT. Assessment of renal function may allow for better informed patient counseling and clinical decision-making. In ESRD patients, the risk of complications from RC may outweigh the potential benefits of adjuvant RT. An alternative approach may be to consider postoperative PSA monitoring for biochemical recurrence in these patients, as opposed to immediate adjuvant therapy. In salvage therapy, thorough counseling regarding the risks of RC and potential benefits of RT may also be necessary. However, further research is needed to establish the safety and efficacy of these approaches.

Preventative measures can also reduce adverse effects from postoperative RT in renal failure patients. One potential approach could implement improved bladder filling protocols prior to RT, as increased bladder volumes have a major impact on both acute and late urinary toxicity [10, 14, 19]. Bladder filling protocols consists of consuming specified amounts of water and not voiding before RT with the goal of producing consistent urine volumes during irradiation and increasing treatment reproducibility [20]. However, patients with severe renal dysfunction may have difficulty achieving adequate bladder volumes, and current protocols provide limited reproducibility of consistent urine volumes [10, 20–22]. Alternative methods of bladder filling, such as active filling, and maintaining consistent bladder volumes at the time of RT should be further explored [21].

The main strength of the present study is that, at this point, it is the first study to investigate the impact of renal function on the development of RC following postoperative RT for prostate cancer. However, our study is not without limitations. While all patients underwent RALP at our single academic institution, some patients received RT at outside hospitals, resulting in greater variability in potential treatment protocols. The high proportion of proton RT patients in our series also limited our study's ability to detect significant differences between proton therapy and other radiation modalities. There was a small number of patients in the CKD 5 group, but despite this limitation, all outcomes remained significant. Patients with CKD 3–4 also demonstrated significantly worse outcomes compared to those with CKD 0–2. These findings will need to be confirmed in future prospective multicenter studies. Lastly, due to the retrospective design of our study, we were unable to measure the bladder volumes of patients at the time of RT. Further well-designed studies quantifying bladder volumes at the time of RT would be of interest.

Conclusion

ESRD is associated with the risk and severity of RC in patients receiving RT following RALP. Knowledge of the potential severity of this complication could guide physicians and patients as they evaluate the risk–benefit ratio prior to selecting adjuvant or salvage RT in this population. Strategies to reduce or avoid RC in ESRD patients should be further investigated.

Acknowledgements No research support was provided from funding agencies or industry.

Funding This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Declarations

Conflict of interest None.

References

1. Kälble T, Lucan M, Nicita G, Sells R, Burgos Revilla FJ, Wiesel M (2005) EAU guidelines on renal transplantation. Eur Urol 47(2):156–166. https://doi.org/10.1016/j.eururo.2004.02.009
2. Chadban SJ, Ahn C, Axelrod DA et al (2020) KDIGO clinical practice guideline on the evaluation and management of candidates for kidney transplantation. Transplantation 104(4S1 Suppl 1):11–103. https://doi.org/10.1097/tp.0000000000003136
3. Litwin MS, Tan H-J (2017) The diagnosis and treatment of prostate cancer: a review. JAMA 317(24):2532–2542

4. Sanguedolce F, Sancho Pardo G, Mercadé Sanchez A et al (2021) Radiation-induced haemorrhagic cystitis after prostate cancer radiotherapy: factors associated to hospitalization and treatment strategies. Prostate Int 9(1):48–53. https://doi.org/10.1016/j.prnil.2020.07.006
5. Martin SE, Begun EM, Samir E, Azaiza MT, Allegro S, Abdelhady M (2019) Incidence and morbidity of radiation-induced hemorrhagic cystitis in prostate cancer. Urology 131:190–195. https://doi.org/10.1016/j.urology.2019.05.034
6. Browne C, Davis NF, Mac Craith E et al (2015) A narrative review on the pathophysiology and management for radiation cystitis. Adv Urol 20:15
7. Makino K, Sato Y, Takenaka R et al (2022) Cumulative incidence and clinical risk factors of radiation cystitis after radiotherapy for prostate cancer. Urol Int 20:1–7. https://doi.org/10.1159/000521723
8. Afonso-João D, Pacheco-Figueiredo L, Antunes-Lopes T et al (2018) Cumulative incidence and predictive factors of radiation cystitis in patients with localized prostate cancer. Actas Urol Españolas (English Ed) 42(4):256–261. https://doi.org/10.1016/j.acuroe.2018.03.006
9. Liem X, Saad F, Delouya G (2015) A practical approach to the management of radiation-induced hemorrhagic cystitis. Drugs 75(13):1471–1482. https://doi.org/10.1007/s40265-015-0443-5
10. Grün A, Kawgan-Kagan M, Kaul D et al (2019) Impact of bladder volume on acute genitourinary toxicity in intensity modulated radiotherapy for localized and locally advanced prostate cancer. Strahlenther Onkol 195(6):517–525. https://doi.org/10.1007/s00066-018-1398-8
11. Chen Z, Yang Z, Wang J, Hu W (2016) Dosimetric impact of different bladder and rectum filling during prostate cancer radiotherapy. Radiat Oncol 11:103. https://doi.org/10.1186/s13014-016-0681-z
12. Allen SD, Thompson A, Sohaib SA (2008) The normal post-surgical anatomy of the male pelvis following radical prostatectomy as assessed by magnetic resonance imaging. Eur Radiol 18(6):1281–1291. https://doi.org/10.1007/s00330-008-0867-3
13. Collado A, Batista JE, Garcia-Penit J, Gelabert A, Arañó P, Villavicencio H (2005) Bladder blood flow and de-obstructive open prostatectomy: correlation with clinical and urodynamic parameters. Int Urol Nephrol 37(1):79–87. https://doi.org/10.1007/s11255-004-6078-1
14. Pinkawa M, Fischedick K, Asadpour B, Gagel B, Piroth MD, Eble MJ (2006) Low-grade toxicity after conformal radiation therapy for prostate cancer—impact of bladder volume. Int J Radiat Oncol Biol Phys 64(3):835–841. https://doi.org/10.1016/j.ijrobp.2005.09.003
15. Nunns GR, Moore EE, Chapman MP et al (2017) The hypercoagulability paradox of chronic kidney disease: the role of fibrinogen. Am J Surg 214(6):1215–1218. https://doi.org/10.1016/j.amjsurg.2017.08.039
16. Helissey C, Cavallero S, Brossard C, Dusaud M, Chargari C, François S (2020) Chronic inflammation and radiation-induced cystitis: molecular background and therapeutic perspectives. Cells 10(1):21
17. Alongi F, Fiorino C, Cozzarini C et al (2009) IMRT significantly reduces acute toxicity of whole-pelvis irradiation in patients treated with post-operative adjuvant or salvage radiotherapy after radical prostatectomy. Radiother Oncol 93(2):207–212. https://doi.org/10.1016/j.radonc.2009.08.042
18. Santos PMG, Barsky AR, Hwang WT et al (2019) Comparative toxicity outcomes of proton-beam therapy versus intensity-modulated radiotherapy for prostate cancer in the postoperative setting. Cancer 125(23):4278–4293
19. Jain S, Loblaw DA, Morton GC et al (2012) The effect of radiation technique and bladder filling on the acute toxicity of pelvic radiotherapy for localized high risk prostate cancer. Radiother Oncol 105(2):193–197. https://doi.org/10.1016/j.radonc.2012.09.020
20. Chen H-H, Lin P-T, Kuo L-T, Lin K-S, Fang C-C, Chi C-C (2021) Bladder volume reproducibility after water consumption in patients with prostate cancer undergoing radiotherapy: a systematic review and meta-analysis. Biomed J 44(6, Supplement 2):226–234. https://doi.org/10.1016/j.bj.2020.11.004
21. Nasser NJ, Fenig E, Klein J, Agbarya A (2021) Maintaining consistent bladder filling during external beam radiotherapy for prostate cancer. Tech Innov Patient Support Radiat Oncol 17:1–4. https://doi.org/10.1016/j.tipsro.2021.01.002
22. Stam MR, van Lin ENJT, van der Vight LP, Kaanders JHAM, Visser AG (2006) Bladder filling variation during radiation treatment of prostate cancer: can the use of a bladder ultrasound scanner and biofeedback optimize bladder filling? Int J Radiat Oncol Biol Phys 65(2):371–377. https://doi.org/10.1016/j.ijrobp.2005.12.039