Original Article

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Association Between Postoperative 3rd Month Renal Function After Radical Cystectomy and Preoperative Factors, Oncologic Outcomes, and Complications

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Abstract

Objective: We aimed to investigate the influence of preoperative factors on postoperative renal function and the association between renal function and oncologic outcomes and complications after radical cystectomy (RC).

Materials and Methods: We retrospectively analyzed patients who underwent RC due to muscle-invasive bladder cancer and intravesical treatment-resistant nonmuscle-invasive bladder cancer in our center between January 2006 and March 2017. The patients' age, gender, comorbidities, preoperative estimated glomerular filtration rate (eGFR), presence of hydronephrosis, hydronephrosis grade and laterality, urinary diversion type, preoperative and postoperative pathology findings, eGFR at postoperative 3rd month, oncologic outcomes, and complication rates were evaluated. The patients were divided into 2 groups based on postoperative eGFR: group 1 (<60 mL/min eGFR) and group 2 (≥60 mL/min eGFR), and data were compared between the groups.

Results: The study included 125 patients with urothelial carcinoma of the bladder who underwent RC and had complete records (59 patients in group 1 and 66 patients in group 2). Of the preoperative factors, only presence of hydronephrosis was significantly higher in group 1 (p=0.012). There were no statistically significant differences between the groups in terms of urinary diversion type, pathology findings, oncologic outcomes, or complications.

Conclusion: Preoperative eGFR and hydronephrosis were significantly associated with postoperative 3rd month eGFR. Postoperative eGFR <60 mL/min was not associated with diversion type, pathologic and oncologic outcomes, or complications.

Keywords: Bladder cancer, postoperative renal function, estimated glomerular filtration rate, radical cystectomy, hydronephrosis

Introduction

Radical cystectomy (RC), extended lymph node dissection, and urinary diversion offer the best survival advantage in the treatment of muscle-invasive bladder cancer (MIBC) and high-risk non-muscle-invasive bladder cancer (NMIBC) (1). However, the need for neoadjuvant chemotherapy (NAC) prior to RC or adjuvant chemotherapy (AC) following RC varies depending on patient characteristics and physician preference (2). For NAC, pre-RC tumor volume (imaging findings consistent with T3 disease and lymph node positivity) and renal function are the important patient-related factors influencing chemotherapy decisions (1,2,3). In contrast, AC is given based on post-RC performance status and renal function (4,5). Although renal functional capacity varies before and after RC, it is important in chemotherapy planning. However, numerous studies have

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demonstrated the relationship between renal function and patients' preoperative characteristics, comorbidities, and presence of hydronephrosis (2,4,5). Risk factors for early postoperative acute renal dysfunction have also been identified (6). However, there are no definitive data regarding the effects of postoperative renal function on post-RC complications (6) and oncologic outcomes.

The aim of this study was to investigate the association between postoperative renal function and preoperative factors, post-RC oncologic outcomes, and complications.

Materials and Methods

Patients with bladder cancer who underwent RC in our center between January 2006 and March 2017 were retrospectively analyzed. Histologic type was urothelial carcinoma in all cases included in the study. Patients with bladder cancers other than urothelial carcinoma, patients with upper urinary tract tumors, obstructive urinary tract stone disease, or solitary kidney prior to RC, patients receiving NAC (due to their small number), and patients with missing follow-up data were excluded. The patients' general characteristics and preoperative, peroperative, and postoperative data were screened. The patient group consisted of those with MIBC and NMIBC (Ta, T1, carcinoma *in situ*). The NMIBC group included Ta patients presenting with extensive, refractory, and frequent hematuria and T1 patients resistant to intravesical therapy.

Patients were analyzed in terms of general characteristics (age, gender, presence of diabetes mellitus (DM), hypertension (HT), and other comorbidities); preoperative data [preoperative estimated glomerular filtration rate (eGFR), American Society of Anesthesiologists (ASA) Score, Eastern Cooperative Oncology Group (ECOG) Performance Score, Charlson Comorbidity Index, and presence, grade, and laterality of hydronephrosis]; peroperative data (operation time, type of urinary diversion); pathologic data (pre- and postoperative T stage, grade, and other important pathology findings); postoperative data (eGFR at postoperative 3rd month); oncologic outcomes (upstaging, AC rate, overall mortality and survival time, and cancer-specific mortality and survival time); and complication data (length of hospital stay, rates of early medical and surgical complications, and distribution of complications according to Clavien-Dindo classification). Hydronephrosis was defined as the presence of dilation of the renal pelvis and calyces and renal pelvic anteroposterior diameter of >10 mm in ultrasonography or computed tomography (7). Based on previous studies, the patients were divided into 2 groups according to a postoperative eGFR threshold of 60 mL/min (6,8,9). Patients with eGFR <60 mL/min were in group 1 and those with eGFR ≥60 mL/min were in group 2.

Statistical Analysis

The data were analyzed using Statistical Package for the Social Sciences, version 20.0 (SPSS, Chicago, IL, USA) software. Patients classified into groups 1 and 2 based on postoperative eGFR level were compared. Univariate analysis was done using Mann-Whitney U test and Pearson's chi-square test; multivariate analysis was done using binary logistic regression analysis. In addition, overall survival and cancer-specific survival data were analyzed using Kaplan-Meier survival analysis and log-rank test. The data in the tables are expressed in median (minimum-maximum) and these values were used for statistical analysis. P value <0.05 was accepted as the level of significance.

Results

A total of 125 patients with urothelial carcinoma of the bladder who underwent RC and had complete records were analyzed. Mean age was 64.1±8.8 (32-83) years and mean follow-up period was 32.4±30.8 (1-113) months; 12 (9.6%) of the patients were female. The mean overall and cancer-specific survival times were 58.7±4.8 and 67.9±5.1 months, respectively. Group 1 included 59 patients and group 2 included 66. Patient characteristics and preoperative data of groups 1 and 2 and the results of comparison between the groups are presented in Table 1. Patient characteristics were similar between the groups. Of the preoperative parameters, preoperative eGFR and hydronephrosis rate were significantly higher in group 1 (p=0.012). Other data affecting eGFR were comparable in the 2 groups. Preoperative, peroperative, and postoperative pathology findings of the groups and their comparative results are given in Table 2. There were no significant differences between the groups in terms of pathology or urinary diversion type. In addition, postoperative pathology results indicated at least stage T1 in all patients who underwent RC due to NMIBC. There were no significant differences in oncologic data or complications between the groups (Table 3). The AC rates of the groups were also similar. The patients showed similar overall survival time (group 1: 57.8±7.0 months and group 2: 54.3±5.7 months, p=0.662) and cancer-specific survival time (group 1: 68.8±7.2 months and group 2: 60.9±6 months, p=0.821) and mortality rates (overall mortality was 49.2% in group 1 and 43.9% in group 2, p=0.560; cancer-specific mortality was 37.3% in group 1 and 34.8% in group 2, p=0.777). The overall and cancer-specific survival curves of the patients are shown in Figures 1 and 2.

Discussion

This study investigated patient characteristics and comorbidities influencing post-RC eGFR at postoperative 3rd month, and ASA Score, ECOG Performance Score, Charlson Comorbidity Index, and the presence of DM, HT, and other comorbidities were found to have no effect on postoperative eGFR. However, we observed a significant correlation between preoperative hydronephrosis and low eGFR (p=0.012). Other than this, the most important factor affecting postoperative eGFR was preoperative eGFR (p<0.001). In a study investigating risk factors for acute renal failure in the early postoperative period (after the withdrawal of ureteral stent on postoperative day 7), acute renal failure was observed in 48 of 145 patients evaluated. In these 48 patients, preoperative eGFR <60, HT, and NAC were identified as independent risk factors for acute renal failure (6). Unlike that study, our study focused on renal function at postoperative month 3 rather than the early postoperative period. In addition, our study did not include patients receiving NAC. In a recent similar study including 164 patients, factors influencing eGFR at postoperative 3rd month were investigated by creating a

Table 1. General characteristics of the patients and the comparison of preoperative data between groups				
		Postoperative eGFR <60 mL/s (Group 1) (n=59)	**Postoperative eGFR ≥60 mL/s (Group 2) (n=66)**	**p**
Age (years)		66 (45-83)	64 (32-80)	0.288
Gender	Female	8	4	0.155
	Male	51	62	
Preoperative eGFR		55.1 (17.5-118.4)	75.3 (6.8-141.4)	<**0.001**
Postoperative 3rd month eGFR		40.4 (15.7-59.3)	82.5 (60.0-118.4)	-
ASA Score	1	2	3	0.756
	2	37	38	
	3	20	24	
	4	0	1	
ECOG Performance Score	0	15	18	0.88
	1	27	31	
	2	10	11	
	3	4	5	
	4	1	0	
Charlson Comorbidity Index	0	0	1	0.241
	1	2	1	
	2	15	9	
	3+	42	55	
DM, n (%)		13 (22)	10 (15.2)	0.322
HT, n (%)		21 (35.6)	27 (40.9)	0.542
Other comorbidity, n (%)		45 (76.3)	46 (69.7)	0.410
Preoperative hydronephrosis	(+)	31 (52.5)	20 (30.3)	**0.012** ***0.012**
	(-)	28 (47.5)	46 (69.7)	
Hydronephrosis laterality	Unilateral	22 (71)	15 (75)	0.753
	Bilateral	9 (29)	5 (25)	
Preoperative grade of hydronephrosis	1	0 (0)	4 (20)	0.074
	2	9 (29)	4 (20)	
	3	16 (51.6)	8 (40)	
	4	6 (19.4)	4 (20)	

ASA: American Society of Anesthesiologists, ECOG: Eastern Cooperative Oncology Group, DM: Diabetes mellitus, HT: Hypertension, eGFR: Estimated glomerular filtration rate
*Binary logistic regression analysis
Mann-Whitney U test and Pearson chi-square test

nomogram (2). It was reported that postoperative eGFR was significantly associated with patient age and preoperative eGFR, as well as type of urinary diversion and thickness of abdominal subcutaneous fat tissue. In addition, the authors emphasized that postoperative eGFR may be improved due to removal of the obstruction after surgery in patients with preoperative hydronephrosis, but the difference was statistically nonsignificant (2). They stated that although postoperative eGFR may be improved in cases of hydronephrosis associated with acute obstructions, eGFR may not improve in patients with long-term, slow-growing obstructions (2). Here, the compensatory capacity of the patient's contralateral kidney is also important.

Our results in the present study differ from the aforementioned findings. Firstly, of 51 patients with hydronephrosis, 31 also had low postoperative eGFR. However, these 51 patients had similar bilateral and unilateral hydronephrosis rates and grade of hydronephrosis in both groups. This may be attributed to the slow progression of hydronephrosis as a chronic process in the bladder, and this leads to permanent renal dysfunction (2). In addition, in the present study, group 1 showed lower postoperative eGFR compared to preoperative values, while an increase was observed in group 2 ($p<0.001$). Thus it can be said that persistent renal dysfunction due to hydronephrosis in this group does not improve postoperatively. The findings of previous research and our study suggest that comorbidities are not associated with poor postoperative renal function, whereas type of urinary diversion must be evaluated further (2,5,8). In terms of early postoperative acute renal failure, no difference in rate was reported with ileal conduit, neobladder,

Table 2. Comparative results of the patients' preoperative, peroperative, and postoperative findings and pathology data				
		Postoperative eGFR <60 mL/s (Group 1) (n=59)	**Postoperative eGFR ≥60 mL/s (Group 2) (n=66)**	**p**
Preoperative T stage	≤T1	6	9	0.835
	T2	51	55	
	T3	2	2	
Preoperative tumor grade	Grade 1	1	2	0.05
	Grade 2	5	0	
	Grade 3	53	64	
CIS	(+)	10	28	0.002
	(-)	49	37	
Squamous differentiation	(+)	9	10	0.984
	(-)	49	55	
Operation time (h)		6 (3-9)	6 (3-8)	0.482
Postoperative T stage	T1	10	16	0.609
	T2	29	26	
	T3	10	10	
	T4	10	14	
Postoperative tumor grade	1	3	5	0.489
	2	1	3	
	3	50	49	
Positive surgical margin	(+)	9	13	0.515
	(-)	50	53	
Number of lymph nodes dissected		12 (1-24)	14 (2-33)	0.197
Number of positive lymph nodes		0 (0-10)	0 (0-8)	0.163
Lymph node positivity	(+)	13	9	0.228
	(-)	44	54	
Percentage of positive lymph nodes		0 (0-70)	0 (0-66.7)	0.154
Prostatic invasion	(+)	7	9	0.831
	(-)	48	55	
Urethral invasion	(+)	3	7	0.258
	(-)	54	57	
Urethral orifice involvement	(+)	13	16	0.770
	(-)	46	50	
Lymphovascular invasion	(+)	11	11	0.799
	(-)	47	53	
Perineural invasion	(+)	7	9	0.745
	(-)	51	55	
Diversion type	Ureterocutaneostomy	25	26	0.735
	Diversion	34	40	

CIS: Carcinoma *in situ*, eGFR: Estimated glomerular filtration rate
Mann-Whitney U test and Pearson chi-square test

and ureterocutaneostomy (6). In the late postoperative period, Thompson et al. (5) reported that advance age, reduced preoperative eGFR, and continent diversion were factors associated with reduced eGFR 3rd month postoperatively. In another study investigating diversion type, 24 patients had ileal neobladder, 12 had ileocecal neobladder, 25 had ileal conduit, and 9 had ureterocutaneostomy. Although patient age, preoperative eGFR, and HT were significant factors in the choice of diversion, type of diversion was found to have no significant effect on long-term renal functions (9). Postoperative episodes of pyelonephritis and AC were identified as among the factors associated with reduced renal function (9). In

Table 3. Comparisons of postoperative data, oncologic outcomes, and complications between the patient groups				
		Postoperative eGFR <60 mL/s (Group 1) (n=59)	Postoperative GFR ≥60 mL/s (Group 2) (n=66)	p
Upstaging	(+)	25	26	0.735
	(-)	34	40	
Stage change	Upstaging	25	26	0.778
	Downstaging	8	12	
	No change	26	28	
Adjuvant chemotherapy, n (%)		17 (28.8)	17 (25.8)	0.701
Overall mortality, n (%)		29 (49.2)	29 (43.9)	0.560
Overall survival (months)		57.8±7.0	54.3±5.7	0.662
Cancer-specific mortality, n (%)		22 (37.3)	23 (34.8)	0.777
Cancer-specific survival (months)		68.8±7.2	60.9±6.0	0.821
Hospital stay (days)		11 (5-29)	11 (5-42)	0.697
Early medical complications	(+)	15	14	0.578
	(-)	44	52	
Early surgical complications	(+)	24	27	0.979
	(-)	35	39	
Clavien-Dindo complication classification	1	3	9	0.172
	2	38	45	
	3a	3	0	
	3b	9	9	
	4a	5	3	
	5	1	0	
eGFR: Estimated glomerular filtration rate Mann-Whitney U test and Pearson chi-square test				

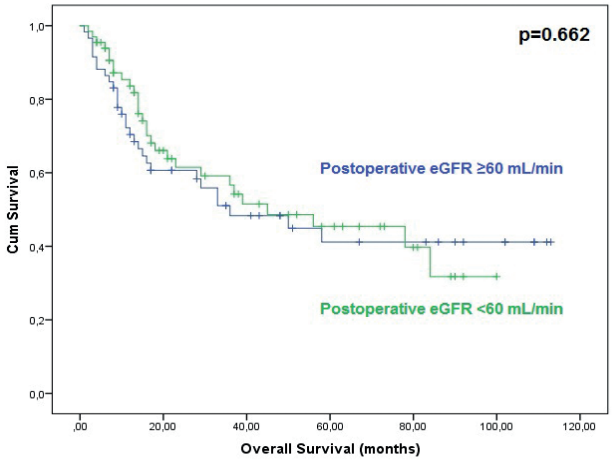

Figure 1. Overall survival analysis curves of patients in groups 1 and 2
eGFR: Estimated glomerular filtration rate

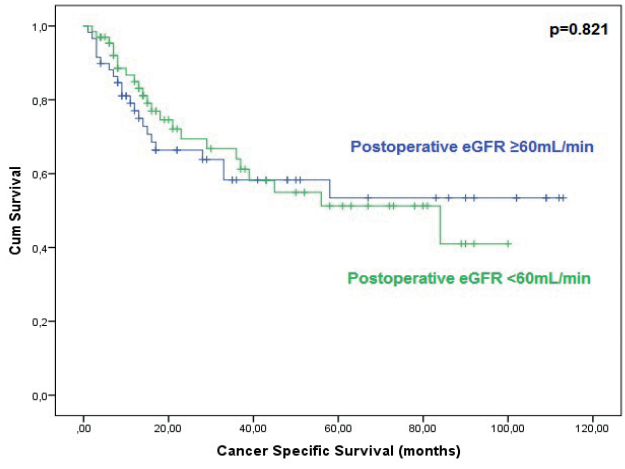

Figure 2. Cancer-specific survival analysis curves of patients in groups 1 and 2
eGFR: Estimated glomerular filtration rate

another study of 68 patients with continent diversion and 47 with incontinent diversion, preoperative eGFR was significantly lower in the incontinent group, while the continent group had a higher proportion of patients with postoperative stage 3B chronic kidney disease (CKD). Significant factors associated with stage 3B CKD at 5 years were advanced age, preoperative eGFR, ureterocutaneostomy, and postoperative hydronephrosis (8). Although our results are consistent with previous studies reporting that comorbidities do not influence renal function, our lack of significant findings regarding diversion type suggests that further investigation into its effect on renal function is warranted. Moreover, while there are some reports that obesity and body mass index (BMI) are associated with postoperative renal function (10,11,12), we were not able to evaluate this in the present study due to incomplete data regarding obesity and BMI.

In our study, preoperative and postoperative pathologic data and operative times of patients were similar at different eGFRs. Analysis of oncologic outcomes showed that upstaging, presence of AC, and overall and cancer-specific survival and mortality rates were also similar at different eGFR. With regard to complication rates, eGFR had similar effects on early medical and surgical complications. Clavien-Dindo complication classification was similar between the groups.

Study Limitations

The most important limitations of this study were the small number of patients, retrospective study design, lack of important data such as BMI, obesity, and preoperative tumor location, and exclusion of patients who received NAC due to their small population.

Conclusion

Our results suggest that postoperative eGFR is significantly associated with preoperative eGFR and hydronephrosis, while the presence of comorbidity is not a significant factor. However, comorbidities may have an effect on preoperative renal function reserve rather than postoperative short-term renal functions. Apart from that, we observed in our study that postoperative eGFR is not associated with type of urinary diversion, pathologic and oncologic outcomes, or complication rates. We believe that larger prospective studies can provide more accurate information.

Ethics

Ethics Committee Approval: Retrospective study.
Informed Consent: Retrospective study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: S.Ç., İ.B., E.Ş., S.Y., İ.H.B., T.Y., B.G., T.D., Concept: S.Ç., İ.B., E.Ş., Design: S.Ç., İ.B., E.Ş., Data Collection or Processing: S.Ç., İ.B., E.Ş., S.Y., Analysis or Interpretation: S.Ç., İ.H.B., T.Y., B.G., T.D., Literature Search: S.Ç., İ.B., E.Ş., Writing: S.Ç.

Conflict of Interest: No conflict of interest was declared by the authors.

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