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ORIGINAL ARTICLE

The renal safety and efficacy of combined gemcitabine plus cisplatin and gemcitabine plus carboplatin chemotherapy in Chinese patients with a solitary kidney after nephroureterectomy

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Abstract
Purpose The renal safety of cisplatin-based chemotherapy has not been investigated in patients with urothelial carcinoma of the upper urinary tract (UUT-UC) who retain a solitary kidney after nephroureterectomy. This study aimed to assess and compare the renal safety and efficacy of gemcitabine–cisplatin (GP) and gemcitabine–carboplatin (GC) in these patients.
Methods The medical records of patients diagnosed with urothelial carcinoma at the Sun Yat-Sen University Cancer Center between January 2005 and December 2015 were retrospectively reviewed. The creatinine clearance (CrCl) and estimated glomerular filtration rate (eGFR) were used to assess renal function and were calculated using different formulas.
Results A total of 71 patients were enrolled in this study; 48 patients were on GP, and 23 were on GC. The renal function indicators (CrCl and eGFR) were all significantly lower after GP chemotherapy than at baseline, a phenomenon that was not observed in the GC group. Severe nephrotoxicities (SNTs) were reported in 12 patients on GP (25%) and zero on GC. SNT risk factors included a more than 20% decrease in eGFR after one GP cycle and the presence of diabetes (all $p < 0.05$). Among patients treated with first-line palliative chemotherapy ($n = 32$), GC ($n = 13$) patients had an ORR of 46.2%, which was not significantly different from GP patients (36.8%, $n = 19$), whereas GC patients tended to have a shorter OS than GP patients (9.2 vs. 29 months, $p = 0.200$).
Conclusions Our results confirm that GP has an adverse impact on the renal function of patients with UUT-UC who retain a solitary kidney, but it can be safely administered to the majority of these patients without inducing SNT. In specific patients, GC is an alternative to GP that has comparable efficacy and favourable renal toxicity.

Keywords Urothelial carcinoma of upper urinary tract (UUT-UC) · Solitary kidney · Chemotherapy · Cisplatin · Carboplatin · Gemcitabine

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Introduction

Urothelial carcinoma of the upper urinary tract (UUT-UC) is a rare malignancy, accounting for approximately 5–10% of all urothelial malignancies [1–3]. Radical nephroureterectomy is the gold standard management and only curable therapeutic option for UUT-UC, although the UUT-UC

prognosis remains poor if invasive [4–6]. Therefore, it is reasonable to advocate for systematic chemotherapy as an adjuvant treatment for locally advanced UUT-UC or as salvage treatment for disseminated disease [7]. However, due to the rarity of these tumours, randomized clinical trials are not available, and data are sparse regarding the use of chemotherapy to treat UUT-UC. Given similar biological features and chemosensitivity to bladder cancer [8, 9], a cisplatin-based regimen is commonly prescribed in the chemotherapy regimen for UUT-UC [10–13].

Recently, a combination of gemcitabine and cisplatin (GP) has become the front-line chemotherapy regimen for bladder cancer as well as UUT-UC [14]. Although GP has shown considerable efficacy in UUT-UCs [15], there is a therapeutic dilemma regarding the utility of GP for treating patients with UUT-UC who retain a solitary functional kidney after nephroureterectomy. The high prevalence of chronic kidney disease [16] and decreased renal reserve due to kidney removal is the major concern [17]. To date, available data on the renal safety of GP chemotherapy in this particular group are rare. In 2011, a group from Korea published a retrospective review of 60 patients with UUT-UC who were treated with cisplatin-based chemotherapy after nephroureterectomy. Their data demonstrated that a cisplatin-containing regimen (GP in 20 patients) was tolerable in the majority of patients with a solitary kidney [18]; however, the study did not provide detailed results for the GP arm.

Carboplatin has a similar mechanism of action as cisplatin but has different pharmacokinetics and relatively low nephrotoxicity [19]. In clinical practice, carboplatin is considered as a substitute for cisplatin in a series of cancers in patients who are unfit for cisplatin. In a randomized study, gemcitabine plus carboplatin (GC) is an effective regimen for patients with urothelial carcinomas, and it is generally considered an alternative to GP in patients with renal impairment [20, 21]. On the basis of this consideration, the GC regimen might be a rational treatment option for patients with UUT-UC after nephroureterectomy. Unfortunately, it remains uncertain whether the renal safety of GP is superior to that of GC in this patient population due to limited available data.

We conducted this study to compare the renal safety of GP and GC in patients who have a solitary kidney after nephroureterectomy as well as to further assess the efficacy of the two regimens. We hope that our results provide important guidance for this particular population of Chinese patients.

Patients and methods

Ethics statement

All of the patients provided written consent for their information to be stored in the Sun Yat-Sen University Cancer Center database and used for research. This study was conducted in accordance with the ethical standards of the World Medical Association's Declaration of Helsinki and approved by an independent ethics committee at the Cancer Center of Sun Yat-Sen University.

Patient selection and treatment

We retrospectively reviewed the medical records of patients who were diagnosed with urothelial carcinoma at the Sun Yat-Sen University Cancer Center between January 2005 and December 2015. Finally, a total of 71 patients who underwent palliative/adjuvant chemotherapy with GP ($n = 48$) or GC ($n = 23$) after nephroureterectomy for UUT-UC were included. All of the patients were chemo naive. Patients who had previously received neoadjuvant chemotherapy and had a definite history of acute or chronic renal disease were excluded. Basic demographics (gender and age), baseline tumour characteristics (location and side of the primary tumour) and relevant laboratory data were collected.

The two chemotherapy regimens were administered every 28 days as follows: 1000 mg/m^2 gemcitabine on days 1, 8 and 15 and 75 mg/m^2 cisplatin on day 1 for the GP regimen and 1000 mg/m^2 gemcitabine on days 1 and 8 and carboplatin AUC × 5 on day 1 for the GC regimen. Gemcitabine was diluted in 100 mL of normal saline and administered as a continuous infusion within 30 min. Cisplatin was diluted in 500 mL of normal saline and administered a continuous infusion over 3 h, while adequate hydration was given. Carboplatin was diluted in 500 mL of 5% glycosylated solution and administered a continuous infusion over 1 h. Chemotherapy was discontinued if the disease progressed or intolerable toxicity developed, according to the physician's evaluation.

Evaluation

Relevant laboratory tests for renal function were performed before and after each chemotherapy cycle. The serum creatinine level, creatinine clearance (CrCl), and estimated glomerular filtration rate (eGFR) were adopted as indicators of renal function. CrCl was calculated using the C–G formula (Cockcroft–Gault) [22], and eGFR was calculated using the CKD-EPI (Chronic Kidney Disease Epidemiology Collaboration formula) [23]. Severe nephrotoxicity (SNT) during the treatment course was identified as ≥grade 2 renal function-related adverse events by the Common Terminology Criteria for Adverse Events (version 3) [24]. The objective tumour response was evaluated by computed tomography every two cycles using the Response Evaluation Criteria in Solid Tumours [25].

Statistical analysis

Comparisons of renal function were displayed with the paired *t* test. Comparisons between proportions were performed with Chi-square or Fisher's exact tests. Logistic regression methodology was used to detect risk factors for SNT. The overall survival (OS) was defined as the time from the date of surgery to the date of death or the last follow-up visit, and it was estimated with the Kaplan–Meier method and compared using the log-rank test. Univariate and multivariate survival analyses were performed based on the Cox proportional hazards regression methodology. Hazard ratios (HRs) with 95% CIs and two-sided *p* values are reported. An alpha value of $p < 0.05$ was considered statistically significant. The statistical analyses were performed using the Statistical Package for the Social Sciences version 19.0(IBM company, Armonk, NY, USA).

Results

Clinico-pathological characteristics

The baseline characteristics of all of the participants are listed in Table 1. The median age of the entire study cohort was 59 years (range 43–73) and contained primarily men. Hypertension and diabetes were observed in 13 patients (18.3%) and 8 patients (11.3%), respectively. Forty-six patients (64.8%) presented with a primary tumour in the renal pelvis, and 25 tumours (35.2%) were located at the urethra. Adjuvant chemotherapy and first-line palliative chemotherapy were administered to 39 (54.9%) and 32 patients (45.1%), respectively. The median number of chemotherapy cycles was three. Baseline clinical characteristics were generally well balanced across the two treatment groups (GP vs. GC), and there were no statistically significant difference.

Renal function

The baseline mean values for serum creatinine (μmol/L), CrCl (mL/min) and eGFR (mL/min/1.73 m^2) were 100.5 ± 23.5, 62.0 ± 17.5 and 69.6 ± 18.6 for GP and 109.6 ± 37.1, 68.1 ± 53.8 and 68.1 ± 29.4 for GC, respectively. There were no significant differences in the four values between GP and GC (all $p > 0.05$, Table 1). Changes in renal function were followed every cycle. For patients in the GP group, the mean serum creatinine (μmol/L) after three cycles of chemotherapy was 107.0 ± 24.2, which is significantly higher than at baseline ($p = 0.012$, Table 2). Likewise, the mean CrCl (mL/min) and eGFR (mL/min/1.73 m^2) values were 61.4 ± 17.3 and 65.9 ± 18.9 after three cycles of GP, respectively, and both were significantly lower than at baseline in the GP group (all $p < 0.05$, Table 2). However, for the GC group, the three renal function indicators did not show any significant change after the third cycle (Table 2).

Toxicity

No toxicity-related death was observed. Febrile neutropenia (FN) occurred in three patients (6.3%) who received GP and one patient who received GC (4.3%), anaemia grade 3/4 in one GP patient and three GC patients (13.0%). Furthermore, thrombopenia grade 3/4 in four GP patients (8.3%) and two GC patients (8.7%), showing no statistical significance between the GP and GC groups (all $p > 0.05$, Table 3). GP is associated with a relatively higher rate of nausea and vomiting grade 3/4 (5/48, 10.4%) than GC (1/23, 4.3%). Most importantly, SNT occurred in 12 patients (25%) on GP, whereas no SRT was observed in the GC group ($p = 0.007$, Table 3). Of 12 patients with SNT, 5 patients developed SNT after the first cycle, and 3 patients developed SNT after the second cycle. After management by a nephrologist, all of the SNT was cured, and no dialysis was needed.

We then performed a multivariate analysis using a regression model in patients receiving GP (Table 4). An over 20% decrease in eGFR (assessed by CKD-EPI) after one cycle and the presence of diabetes were two risk factors for SNT (all $p < 0.05$). However, the gender, age, baseline serum creatinine, baseline CrCl and eGFR levels, resected kidney, hypertension and aims of chemotherapy were not associated with SNT.

Treatment response and survival

Palliative chemotherapy was provided to 32 patients, although complete response (CR) was not observed. Partial response (PR) was observed in 7 patients (36.8%) on GP and 6 patients (46.2%) on GC (Table 3). In addition, OS was evaluated for the two groups ($n = 32$). Within a median follow-up time of 16 months, 14 deaths were observed (7 on GP and 7 on GC). The 2-year OS rate and median OS time were 50.6% and 29.0 months for GP and 38.1% and 9.2 months for GC, respectively ($p = 0.200$, Fig. 1).

Discussion

To the best of our knowledge, this is the first study evaluating GP and GC regimens in patients with solely UUT-UC and a solitary kidney. A statistically significant reduction in renal function (evaluated by CrCl and eGFR) was

Table 1 Baseline characteristics for all patients

Variables	Overall ($n = 71$)		GP ($n = 48$)		GC ($n = 23$)		p value
	No.	%	No.	%	No.	%	
Age (years)							
Median (range)	59 (43–73)		57 (43–72)		61 (44–73)		0.134
Mean ± SD	58.3 ± 7.5		57.4 ± 7.3		60.2 ± 7.7		
Gender							
Male	56	78.9	35	72.9	21	91.3	0.120
Female	15	21.1	13	27.1	2	8.7	
Hypertension							
Presence	13	18.3	7	14.6	6	26.1	0.327
Absence	58	81.7	41	85.4	17	73.9	
Diabetes mellitus							
Presence	8	11.3	6	12.5	2	8.7	1.000
Absence	63	88.7	42	87.5	21	91.3	
Primary tumour							
Ureter	25	35.2	17	35.4	8	34.8	1.000
Renal pelvis	46	64.8	31	64.6	15	65.2	
Resected kidney							
Left	33	46.5	21	43.8	12	52.2	0.613
Right	38	53.5	27	56.3	11	47.8	
T stage							
pT1	3	4.2	2	4.2	1	4.3	0.511
pT2	10	14.1	7	14.6	3	13.0	
pT3	34	47.9	23	47.9	11	47.8	
pT4	15	21.1	12	25.0	3	13.0	
pTx	9	12.7	4	8.3	5	21.7	
N stage							
pN0	35	49.3	24	50.0	11	47.8	0.985
pN+	24	33.8	16	33.3	8	34.8	
pNx	12	16.9	8	16.7	4	17.4	
Tumour grade							
Unknown	6	8.5	6	12.5	0	0.0	0.339
Grade 1	3	4.2	2	4.2	1	4.3	
Grade 2	4	5.6	3	6.3	1	4.3	
Grade 3	58	81.7	37	77.1	21	91.4	
Aims of chemotherapy							
Adjuvant	39	54.9	29	60.4	10	43.5	0.210
First-line	32	45.1	19	39.6	13	56.5	
Cycles							
Median (range)	3 (1–9)		3 (1–8)		3 (1–9)		0.643
Albumin (g/L)							
Median (range)	39.7 (27.7–75.8)		40.9 (27.7–75.8)		38.9 (28.8–73.9)		0.916
Serum creatinine (μmol/L)							
Median (range)	105 (21.5–187.6)		103 (56.6–161.5)		114 (21.5–187.6)		0.212
Creatinine clearance (mL/min)							
Median (range)	56.6 (31.6–303.6)		57.2 (38.2–109.9)		54.4 (31.6–303.6)		0.478
Estimated GFR (mL/min/1.73 m^2)							
Median (range)	65.3 (31.9–168.7)		65.9 (39.8–111.5)		60.8 (31.9–168.7)		0.799

GP gemcitabine plus cisplatin, *GC* gemcitabine plus carboplatin, *SD* standard deviation, *GFR* glomerular filtration rate

Table 2 Comparison of three indicators of renal function at baseline and after chemotherapy

	GP ($n = 48$)		CBP ($n = 23$)	
	Mean ± SD	p value[a]	Mean ± SD	p value[a]
Serum creatinine (μmol/L)				
Baseline	100.5 ± 23.5		109.6 ± 37.1	
After first cycle	108.7 ± 25.3	0.018*	107.8 ± 25.3	0.745
After second cycle	108.2 ± 21.2	0.010*	106.2 ± 24.8	0.442
After third cycle	107.0 ± 24.2	0.012*	114.0 ± 27.7	0.214
After fourth cycle	99.7 ± 17.9	0.036*	105.3 ± 34.7	0.449
After fifth cycle	104.1 ± 20.1	0.015*	133.3 ± 48.1	0.780
After sixth cycle	106.5 ± 22.1	0.028*	118.8 ± 36.2	0.515
Creatinine clearance (mL/min)				
Baseline	62.0 ± 17.5		68.1 ± 53.8	
After first cycle	57.5 ± 15.0	0.010*	59.2 ± 13.9	0.351
After second cycle	58.2 ± 17.6	0.018*	59.3 ± 13.7	0.323
After third cycle	61.4 ± 17.3	0.006*	58.3 ± 19.3	0.311
After fourth cycle	64.1 ± 16.2	0.019*	63.8 ± 24.1	0.409
After fifth cycle	59.6 ± 14.7	0.007*	70.4 ± 24.1	0.945
After sixth cycle	55.6 ± 6.0	0.027*	69.5 ± 12.8	0.553
Estimated GFR (mL/min/1.73 m^2)				
Baseline	69.6 ± 18.6		68.1 ± 29.4	
After first cycle	63.6 ± 15.5	0.012*	66.4 ± 17.1	0.459
After second cycle	63.9 ± 17.0	0.011*	66.8 ± 17.8	0.388
After third cycle	65.9 ± 18.9	0.017*	62.6 ± 20.1	0.245
After fourth cycle	68.8 ± 18.4	0.035*	69.7 ± 24.5	0.481
After fifth cycle	61.3 ± 13.4	0.009*	59.7 ± 27.6	0.989
After sixth cycle	55.6 ± 5.6	0.028*	64.3 ± 19.1	0.536

GP gemcitabine plus cisplatin, *GC* gemcitabine plus carboplatin, *GFR* glomerular filtration rate

* $p < 0.05$

[a] Compared with baseline

observed in 48 patients after GP chemotherapy was not observed in GC. Moreover, 25% of 48 patients ($n = 12$) developed severe nephrotoxicity (SNT) in the GP group, whereas none was reported in the GC group. These finding implied that GP could be safely administered to in most cases; however, GC had more reliable renal safety in this frail patient population.

The GP combination showed favourable efficacy and toxicity in patients with urothelial carcinoma, with ORRs ranging from 41 to 57% [20, 26]. The role of GP in standard care for urothelial carcinoma has been strengthened by a randomized study from America [27, 28]. Currently, GP has become the standard chemotherapy regimen for UUT-UCs as either adjuvant or salvage treatment [10, 11, 29, 30]. However, GP remains problematic in elderly patients and those with chronic kidney disease, who are generally considered "unfit" for cisplatin due to its renal toxicity. In addition, nephroureterectomy is commonly performed in UUT-UC and is widely considered to significantly impair renal function, as demonstrated by both Eastern and Western colleagues [31–33]. For this particular population, it remains unclear whether the participants could tolerate GP. Given the rarity of UUT-UC, a prospective study was difficult to conduct. Thus far, only one retrospective study from Korea has contributed limited data. In 2011, Korean oncologists reported their experience of 60 patients who were treated with cisplatin-based chemotherapy after radical nephroureterectomy (20 patients on GP). In that study, renal function tended to diminish after chemotherapy, but no detailed data regarding GP were provided. Five of 20 patients (25.0%) on GP ultimately experienced serious renal-related adverse events (AEs) (≥grade 2). In this study, GP was not used as an adjuvant treatment, and risk factors of severe renal toxicity in GP were not identified.

Nephrotoxicity is a serious and dose-accumulating toxicity of cisplatin [34, 35]. A total dose of cisplatin >400 mg was reported to be significantly related with decreased eGFR [36], implying that nephrotoxicity probably occurs when the patient has finished four cycles of cisplatin-containing chemotherapy. Similarly, dosage of cisplatin reduced especially after fifth and sixth cycles due to nephrotoxicity in the current study. Furthermore, our study revealed two SNT risk factors in patients treated with GP, including diabetes and a significant eGFR reduction (≥20%) after one cycle. These results suggested that patients with diabetes should be cautiously given GP. Indeed, diabetes is generally related to early renal function decline and might increase kidney sensitivity to renal toxicity from cisplatin [37]. In addition, dynamic eGFR monitoring was beneficial for the early detection of high-risk SNT patients. For patients presenting with ≥20% reduction of eGFR after one cycle, stopping GP chemotherapy would likely prevent SNT. Besides, biomarkers which could detect cisplatin-related nephrotoxicity in a early phase is warranted. Urinary vanin-1 was recently recognized as an early predictor for eGFR decline in patients treated with cisplatin. In a pilot study by Hosohata et al. [38], significant elevation of urinary vanin-1 on day 3 after cisplatin could predict the elevation of serum creatinine on day 6 in a group of urothelial carcinoma patients. For the patients with a solitary kidney, urinary vanin-1 might help to detect nephrotoxicity in an early phase and to further prevent SNT.

With regard to toxicity profiles other than nephrotoxicity, no significant differences between other

Table 3 Efficacy and toxicities

Variables	GP		GC		*p* value
	No.	%	No.	%	
Treatment response					
CR	0	0.0	0	0.0	0.863
PR	7	36.8	6	46.2	
SD	10	52.6	6	46.2	
PD	2	10.6	1	7.7	
Severe nephrotoxicity					
Presence	12	25.0	0	0.0	0.007*
Absence	36	75.0	23	100.0	
Nausea and vomiting					
0–2	43	89.6	22	95.7	0.656
3–4	5	10.4	1	4.3	
FN					
Presence	3	6.3	1	4.3	1.000
Absence	45	93.7	22	95.7	
Anaemia					
0–2	47	97.9	20	87.0	0.097
3–4	1	2.1	3	13.0	
Thrombopenia					
0–2	44	91.7	21	91.3	1.000
3–4	4	8.3	2	8.7	

GP gemcitabine and cisplatin, *GC* gemcitabine and carboplatin, *CR* complete response, *PR* partial response, *SD* stable disease, *PD* progression disease, *FN* febrile neutropenia

* $p < 0.05$

Table 4 Risk factors for the development of severe nephrotoxicity

Variables	Hazard ratio (95% CI)	*p* value
Gender		
Male vs. female	0.134 (0.007–2.737)	0.192
Age		
≤57 vs. >57 years	1.010 (0.837–1.218)	0.919
Aims of chemotherapy		
Adjuvant vs. palliative	0.632 (0.066–6.004)	0.689
Reduction of eGFR after 1st cycle		
>20 vs. ≤20%	58.081 (1.438–2345.573)	0.031*
Diabetes		
Presence vs. absence	38.746 (1.038–1446.376)	0.048*
Hypertension		
Presence vs. absence	1.150 (0.083–15.856)	0.917
Resected kidney		
Left vs. right	0.351 (0.041–3.029)	0.341
Serum creatinine (μmol/L)		
≤103 vs. >103	2.054 (0.031–135.763)	0.736
Creatinine clearance (mL/min)		
≥57.2 vs. <57.2	3.701 (0.252–54.315)	0.340
Estimated GFR (mL/min/1.73 m^2)		
≥65.9 vs. <65.9	1.505 (0.040–56.809)	0.825

CI confidence interval, *SD* standard deviation, *GFR* glomerular filtration rate

* $p < 0.05$

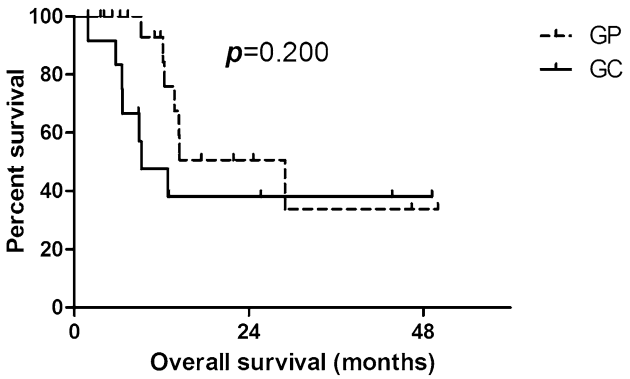

Fig. 1 Kaplan–Meier curves for the overall survival (OS) in GP and GC

non-haematological toxicities and haematological toxicities were detected between GP and GC. No treatment-related deaths were reported. GP showed a relatively higher rate of nausea and vomiting grade 3/4 and a relatively lower rate of anaemia grade 3/4, but these differences were not statistically significant.

Carboplatin has long been recognized as a promising substitute for cisplatin in patients with renal impairment [1–3]. Therefore, it is logical to study gemcitabine plus carboplatin (GC) to treat patients with urothelial carcinoma. Nogué-Aliguer et al. studied the tolerance and activity of GC in 31 patients with UUT-UCs and identified a response rate of 56.1% in 2003 [39]. In 2007, an Italian group demonstrated that GC showed a comparable response rate of 40% and acceptable toxicity profiles with GP from a randomized phase II study [20]. In 2009, EORTC study 30986 revealed that GC exhibited considerable activity, with a response rate of 42%, in advanced urothelial cancer patients who were unfit for cisplatin. However, GC was only effective in 26% of high-risk patients [21]. Park et al. conducted a retrospective study evaluating GC efficacy and toxicity in 31 patients with UUT-UCs who were unfit for cisplatin [40]. All of the patients included in that study met one of the following criteria: Eastern Cooperative Oncology Group (ECOG) performance status ≥2, age ≥75 years or eGFR <60 mL/min. GC achieved a 45.1% response rate, and favourable toxicity was observed in these patients. The combination of ifosfamide, carboplatin and etoposide (ICE) has also been safely used in patients after nephrourectomy in a previous study [41]. However, no results with respect to GC in UUT-UC patients with a solitary kidney have yet

been reported. In this study, renal safety was retrospectively compared between GP and GC in a compromised patient population for the first time. Our study validated that GC has a renal safety advantage and comparable toxicity, other than nephrotoxicity, compared to GP. Among patients treated with first-line palliative chemotherapy ($n = 32$), GC ($n = 13$) did not have a significantly different ORR (36.8%) from that of 46.2% in GP ($n = 19$). In Fig. 1, we could easily find that the survival curve of GC descended earlier than GP and GC reached a much shorter median OS than GP (9.2 vs. 29 months). However, the two curves (GP and GC) eventually crossed and stayed parallel to 48 months; thus, the significant difference was not obtained in the log-rank test ($p = 0.200$). The data on efficacy and survival might be limited by the small sample size. The long-term survival of GC should be further evaluated in a prospective study.

GFR is widely accepted as the most valuable and reasonable overall indicator of renal function. However, direct GFR measurements assessed using filtration markers (inulin, ^{125}I-iothalamate, etc.) are expensive and difficult to operate in routine clinical practice [42, 43]. Therefore, various formulas have been established to calculate the GFR, but the suitability of these formulas for cancer patients is unclear, especially for those undergoing cisplatin-based chemotherapy [44]. Ganesh et al. retrospectively examined 208 patients with bladder cancer who received cisplatin-based chemotherapy and calculated the CrCl using various formulas [44]. The authors found that the CrCl calculated from these formulas tended to underestimate true patient renal function, especially in older patients (>65 years). Japanese colleagues explored the validity of renal function calculated using the CKD-EPI equation [23], a Japanese equation, the C–G formula and CrCl measured by a 24 h creatinine collection in 50 patients treated with cisplatin. The CKD-EPI equation was more applicable to these patients than the results from C–G formula and 24 h creatinine collection [43]. In this study, we employed two different formulas (C–G and CKD-EPI) and both of which consistently showed decreased eGFR after GP treatment.

In addition to patients with nephroureterectomy benefitting from our results, patients with unilateral renal atrophy or unilateral non-functional kidney could benefit from our experience. However, the limitations of this study should also be acknowledged. First, this was a retrospective study that was limited to single institute and a small number of patients. Second, because we indirectly measured GFR, these data might not reflect true renal function. Finally, data on renal function after long-term follow-up were not available for analysis. All of the drawbacks should be addressed in a multicentre study with a prospective design in the future.

Conclusions

In conclusion, as far as we know, this is the first study to evaluate the renal safety and efficacy of GP and GC in UUT-UC patients with a solitary kidney after nephroureterectomy. Our results confirm that GP decreases renal function in this particular patient population but can be safely applied to the majority of these patients without inducing SNT. We also demonstrate the favourable renal safety and considerable efficacy of GC. In addition, GC is an alternative to GP for selected UUT-UC patients with a solitary kidney, especially when they are at risk of SNT from GP.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no competing interests.

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