Is the extirpative surgery for primary tumor helpful for the patients with metastatic urothelial cancer at the time of diagnosis?

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Abstract

The stagnant mortality rates for metastatic urothelial cancer (UC) have provoked efforts to find novel treatments. To test the utility of the extirpative surgery for primary tumor as an option for these patients, we investigated the perioperative and oncologic outcomes of surgery for primary tumors in metastatic UC patients.

We reviewed the medical records of 130 metastatic UC patients (bladder: 88, upper tract UC: 42) at diagnosis from November 2005 to November 2016. A total of 56 patients (surgery group) underwent chemotherapy with extirpative surgery for the primary tumor, and 74 patients (non-surgery group) received chemotherapy. We evaluated perioperative outcomes, cancer-specific survival (CSS), and overall survival (OS) using Kaplan-Meier methods and factors related to OS and CSS using Cox regression models.

Surgery group showed similar perioperative outcome and postoperative complications to those previously reported in UC patients without metastasis, and fewer urinary complications than non-surgery group. Surgery group showed better oncological outcomes than non-surgery group for median CSS (16.0 vs 10.0 months, $P=0.014$) and median OS (14.0 vs 9.0 months, $P=0.043$). Multivariate analysis showed Eastern Cooperative Oncology Group performance status and metastasis to liver as significant predictors of CSS and OS. Surgery was not related with OS, but a significant predictor of CSS.

Extirpative surgery for primary tumor in metastatic UC can be feasible and it might have survival benefits, especially those patients with a tolerable general condition and no liver metastasis. In addition, LT reduces the possibility of a surgical procedure towing to urinary complications.

Abbreviations: BCa = bladder cancer, BMI = body mass index, CSS = cancer-specific survival, ECOG = Eastern Cooperative Oncology Group, LN = lymph node, LT = local treatment, OS = overall survival, UC = urothelial carcinoma, UTUC = upper tract urothelial carcinoma.

Keywords: metastasis, nephroureterectomy, radical cystectomy, urothelial carcinoma

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1. Introduction

Bladder cancer (BCa) is the most common malignancy in the urinary tract and ninth most common cancer worldwide.[1] In Korea, 3762 patients were newly diagnosed with and 1280 died from BCa in 2013.[2] In contrast, upper tract urothelial carcinoma (UTUC) is a relatively rare malignancy; for example, the incidence of UTUC has been reported as 2 per 100,000 persons in the United States.[3] Within these groups, the disease in 5% to 15% of patients with BCa[4] and 8% to 30% of patients with UTUC[3,5] had metastasized at the time of diagnosis. Although studies have identified several novel therapeutic targets for the development of systemic therapies[6] and immune checkpoint inhibitors,[7] there has been little improvement in the mortality rates of metastatic disease since the introduction of cisplatin-based combination chemotherapy >20 years ago.[8]

There are many studies that indicate cytoreductive surgery for primary tumor improves survival in some situations of metastatic carcinoma, such as renal cell carcinoma, colon cancer, and ovarian cancer.[9–11] Also, although androgen deprivation therapy is regarded as the standard treatment in patients with metastatic prostate cancer, recent studies indicate that local treatment (LT) such as prostatectomy or radiotherapy is related to increased overall survival (OS) in metastatic prostate cancer patients.[12]

Although the role of LT has been widely studied in many cancers, there are few studies about LT in cases of metastatic urothelial carcinoma (UC). Historically, combination chemotherapy has been the standard treatment option for metastatic UC,[13] and surgery or radiotherapy has been considered only with palliative intention to control the intractable symptoms owing to disease progression. However, the median survival is reported as only approximately 14 months, although cisplatin-based combination chemotherapy has improved the survival of patients with metastatic UC.[14,15]

In this situation, some recent population studies have evaluated whether LT had benefit for metastatic BCa and reported that high-intensity LT (radical cystectomy of bladder or treatments with radiotherapy dose of ≥50 Gy) improves OS in patients with metastatic BCa.[16,17] Considering these reports, our aim was to assess the feasibility and impact of extirpative surgery for primary tumor on OS and cancer-specific survival (CSS) in patients with metastatic UC. Moreover, we evaluated whether the surgery for primary tumor could reduce urinary tract complications caused by disease progression (eg, hematuria, obstruction, or urinary retention[18]).

2. Materials and methods

2.1. Patient selection

We reviewed the records of 135 patients who were initially diagnosed with various forms of metastatic UC in our institution from November 2005 to November 2016. All patients were histologically diagnosed with UC by biopsy or operation (eg, transurethral resection of bladder tumor, cystoscopic bladder biopsy, or ureteroscopic biopsy) and they had distant metastasis in preoperative imaging such as abdomino-pelvic computed tomography (CT), chest CT, bone scan, or positron emission tomography. Patients with only regional lymph node (LN) involvement without distant metastasis were excluded. Two patients with brain metastasis or carcinomatosis and 3 patients with unavailable clinical information were excluded. Of the 130 patients who were included in the analysis (bladder: 88, upper tract UC: 42), 56 underwent chemotherapy with extirpative surgery for primary tumor. The other 74 patients who received chemotherapy were assigned to the non-surgery group. The decision as to treatment method was left to the physician's clinical judgement after discussion with the patient regarding the probable benefits and adverse effects of each treatment.

The TNM stage was determined according to the guidelines in the 8th edition of the *American Joint Committee on Cancer Staging Manual*.[19] Other clinical characteristics, including sex, age, body mass index (BMI), Eastern Cooperative Oncology Group (ECOG) performance status, smoking status, and urinary complications, were investigated by reviewing medical records. Urinary complications were defined as problems in the urinary tract owing to disease progression, and only the cases that required surgical intervention were investigated for our analysis.

2.2. Treatments and follow-up

Patients in the surgery group underwent chemotherapy after extirpative surgery. Chemotherapy regimens were either gemcitabine and cisplatin (or carboplatin in patients unfit for cisplatin) or MVAC (methotrexate, vinblastine, doxorubicin, and cisplatin). The period of the chemotherapy and regimen changes were made according to the treatment response and performance status of the patients and were left to the judgment of the clinicians.

Information on survival status and cause of death was obtained from the National Cancer Registry Database and our institutional electronic medical records. The OS was defined as the period from the first diagnosis of UC to the date of all-cause death. CSS was determined by the date of cancer-specific death or censoring.

2.3. Statistical analysis

Patient clinical characteristics between the 2 study groups were compared using the Mann–Whitney U test for continuous data and χ^2 test for dichotomous variables. Categorical variables were described with frequency and percentages, and continuous variables were described with medians and interquartile range (IQR). Kaplan-Meier methods with a log-rank test were used to evaluate OS and CSS between 2 groups. Factors related to CSS were determined using Cox proportional hazard models. Variables for multivariate analysis were selected by univariate analyses. Comparisons with significance levels of $P < .05$ were considered statistically significant. All statistical analyses were performed using SPSS software, version 23.0 (IBM Corp., Armonk, NY). All statistical tests were 2-tailed, and a P value $< .05$ was considered statistically significant.

2.4. Good clinical practice protocols

This study was performed in agreement with the applicable laws and regulations, good clinical practices, and ethical principles described in the Declaration of Helsinki. This study protocol was approved by the institutional review board of the hospital (approval number: 4–2018–0214).

3. Results

The demographic characteristics of all the patients are shown in Table 1. There were more patients with liver metastasis in the non-surgery than in the surgery group (17.6% vs 3.6%, respectively; $P = .013$). And patients with UTUC were more likely to receive surgery than those with BCa (57.1% vs 36.4%, respectively; $P = .025$). Moreover, patients who had to receive surgical intervention because of urinary tract complications were more prevalent in the non-surgery group than the surgery group (27.0% vs 1.8%, respectively; $P < .001$).

Table 2 shows the perioperative outcomes and pathological characteristics of 56 patients with metastatic UC treated with surgery for primary tumor. The median (interquartile range [IQR]) operating time was 272 (196–378) minutes and 221 (171–258) minutes in radical cystectomy and nephroureterectomy group, respectively. The median estimated blood loss was 850 (600–1580) mL and 400 (205–875) mL, the median (IQR) length of hospitalization was 13 (10–17) days and 7 (5–11) days in each group, respectively. Sixteen patients (50.0%) of radical cystectomy group and 5 patients (20.8%) of nephroureterectomy group received blood transfusion. Two patients (6.2%) and 1 patient (3.1%) in radical cystectomy group experienced grade 3 and 4 postoperative complications by 30 days, respectively. Two patients (6.2%) underwent wound closure owing to wound dehiscence, 1 (3.1%) needed general anesthesia, and 1 patient received had unplanned intensive care unit admission because of hemodynamic instability.

Table 1
Patient characteristics.

Characteristics	Total 130	Non-surgery 74	Surgery 56	P
Sex (%)				.383
Male	109 (83.8%)	64 (86.5%)	45 (80.4%)	
Female	21 (16.2%)	10 (13.5%)	11 (19.6%)	
Age, median (IQR), y	64 (58–70)	66 (58–73)	63 (57–68)	.11
BMI, median (IQR), kg/m^2	23.02 (21.63–24.93)	23.07 (21.71–25.31)	23.00 (21.63–24.79)	.691
ECOG				.038
≤1	87 (66.9%)	44 (59.5%)	43 (76.8%)	
≥2	43 (33.1%)	30 (40.5%)	13 (23.2%)	
Smoking				.026
Nonsmoker	53 (40.8%)	24 (32.4%)	29 (51.8%)	
Current or former smoker	77 (60.2%)	50 (67.6%)	27 (48.2%)	
Primary tumor				.025
Bladder	88 (67.7%)	56 (75.7%)	32 (57.1%)	
Ureter and renal pelvis	42 (32.3%)	18 (24.3%)	24 (42.9%)	
Clinical T stage				.076
≤cT2	20 (15.4%)	15 (20.3%)	5 (8.9%)	
≥cT3	110 (84.6%)	59 (79.7%)	51 (91.1%)	
Clinical N stage				.043
N0	35 (26.9%)	25 (33.8%)	10 (17.9%)	
≥cN1	95 (73.1%)	49 (66.2%)	46 (82.1%)	
LN involved	59 (45.4%)	39 (52.7%)	20 (35.7%)	.054
Lung involved	50 (38.5%)	24 (32.4%)	26 (46.4%)	.104
Bone involved	52 (40.0%)	33 (44.6%)	19 (33.9%)	.219
Liver involved	15 (11.5%)	13 (17.6%)	2 (3.6%)	.013
Visceral involved	98 (75.4%)	54 (73.0%)	44 (78.6%)	.463
Tumor variant	14 (10.8%)	7 (9.5%)	7 (12.5%)	.58

BMI = body mass index, ECOG = Eastern Cooperative Oncology Group, IQR = inter-quartile range, LN = lymph node.

The surgical interventions required for urinary tract complications in each group are shown in Table 3. Twenty patients in the non-surgery group needed surgical intervention because of intractable hematuria, ureteral obstruction, or bladder outlet

Table 2
Perioperative and pathological characteristics of patients with metastatic urothelial carcinoma treated with surgery for primary tumor.

	Radical cystectomy (n = 32)	Nephroureterectomy (n = 24)
Median operating time (IQR), min	272 (196–378)	221 (171–258)
Median estimated blood loss (IQR), mL	850 (600–1580)	400 (205–875)
Blood transfusion (%)	16 (50.0%)	5 (20.8%)
Median hospital stays (IQR), days	13 (10–17)	7 (5–11)
Postoperative complications, n (%)*		
1	7 (21.9%)	2 (8.3%)
2	4 (12.5%)	2 (8.3%)
3a	1 (3.1%)	0 (0.0%)
3b	1 (3.1%)	0 (0.0%)
4	1 (3.1%)	0 (0.0%)
5	0 (0.0%)	0 (0.0%)
Type of urinary diversion, n (%)		
Ureterocutaneostomy	3 (9.4%)	
ICUD	28 (87.5%)	
Neobladder	1 (3.1%)	
Pathologic T stage, n (%)		
2	5 (15.6%)	0 (0.0%)
3	8 (25.0%)	7 (29.2%)
4	19 (59.4%)	17 (70.8%)
Pathologic N stage, n (%)		
pN0	6 (18.7%)	1 (4.2%)
pN1	20 (62.5%)	1 (4.2%)
pN2	3 (9.4%)	5 (20.8%)
pNx	3 (9.4%)	17 (70.8%)
Median removed LN (IQR)†	17 (9–25)	5.5 (3.5–8)

ICUD = ileal conduit urinary diversion, IQR = interquartile range, LN = lymph node.
* Complications according to Clavien–Dindo classification system.
† Data of patients who underwent lymph node dissection.

Table 3
Urinary tract complications requiring surgical procedure.

Complications	Non-surgery 20 (27.0%)	Surgery 1 (1.8%)	P <.001
Hematuria			
Cystoscopic cauterization	4 (5.4%)	0 (0.0%)	
Obstructive uropathy			
Double J stent indwelling	8 (10.8%)	0 (0.0%)	
PCN	6 (8.1%)	1 (1.8%)	
Urinary retention			
Suprapubic cystostomy	2 (2.7%)	0 (0.0%)	

PCN = percutaneous nephrostomy.

obstruction. In contrast, only 1 patient needed surgical intervention for ureteral obstruction in the surgery group.

At a median follow-up of 13 months (IQR = 6–22 months), 121 patients died (112 of UC). Kaplan–Meier curves (Fig. 1) showed that median CSS was significantly longer in surgery group (16.0 [IQR, 10.0–27.0] vs 10.0 [IQR, 4.0–21.0] months, P = .014, respectively). And median OS was also longer in surgery group versus non-surgery group (14.0 [IQR, 10.0–25.0] vs 9.0 [IQR, 4.0–21.0] months; P = .043, respectively). Multivariate analysis demonstrated that higher ECOG (hazard ratio [HR] = 2.001, 95% confidence interval [CI] = 1.313–3.050, P = .001) and metastasis to liver (HR = 2.147, 95% CI = 1.210–3.807, P = .009) were associated with worse CSS. Surgery (HR = 0.663, 95% CI = 0.449–0.980, P = .039) seemed to improve CSS in patients with metastatic UC (Table 4). In the context of OS, multivariate analysis revealed that higher ECOG (hazard ratio [HR] = 2.129, 95% confidence interval [CI] = 1.423–3.185, P < .001) and liver metastasis (HR = 2.161, 95% CI = 1.227–3.807, P = .008) were associated with worse OS. However, surgery (HR = 0.723, 95% CI = 0.500–1.055, P = .093) was not related to OS (Table 5).

Considering the effect of metastatic lesions on survival, only liver involvement was confirmed to be related to CSS (HR = 2.147, 95% CI = 1.210–3.807, P = .009) and OS (HR = 2.161, 95% CI = 1.227–3.807, P = .008). Interestingly, visceral metastasis was not associated with CSS (HR = 0.972, 95% CI = 0.964–3.086, P = .066) or OS (HR = 0.1.023, 95% CI = 0.892–1.541, P = .915).

4. Discussion

The EAU guideline on metastatic UC recommends the use of cisplatin-containing combination chemotherapy, such as gemcitabine and cisplatin or MVAC (methotrexate, vinblastine, doxorubicin, cisplatin).[13,19] The initial response rate of chemotherapy is 50% to 60%, complete responses are reported as 20% in metastatic BCa, and 5-year OS rate is <15%.[15,20] In cases of UTUC, the initial complete response rate of combination chemotherapy has been reported as up to 30%, but almost all patients experience relapse or disease progression.[21] Although novel immune therapy such as atezolizumab has been used to manage advanced or metastatic UC,[22,23] the survival rate of patients with metastatic UC has not been improved dramatically since the early 1990s when cisplatin-containing combination chemotherapy was introduced.[13] In light of these reports, it may be necessary to reconsider the role of LT on primary tumors in the patients with metastatic UC.
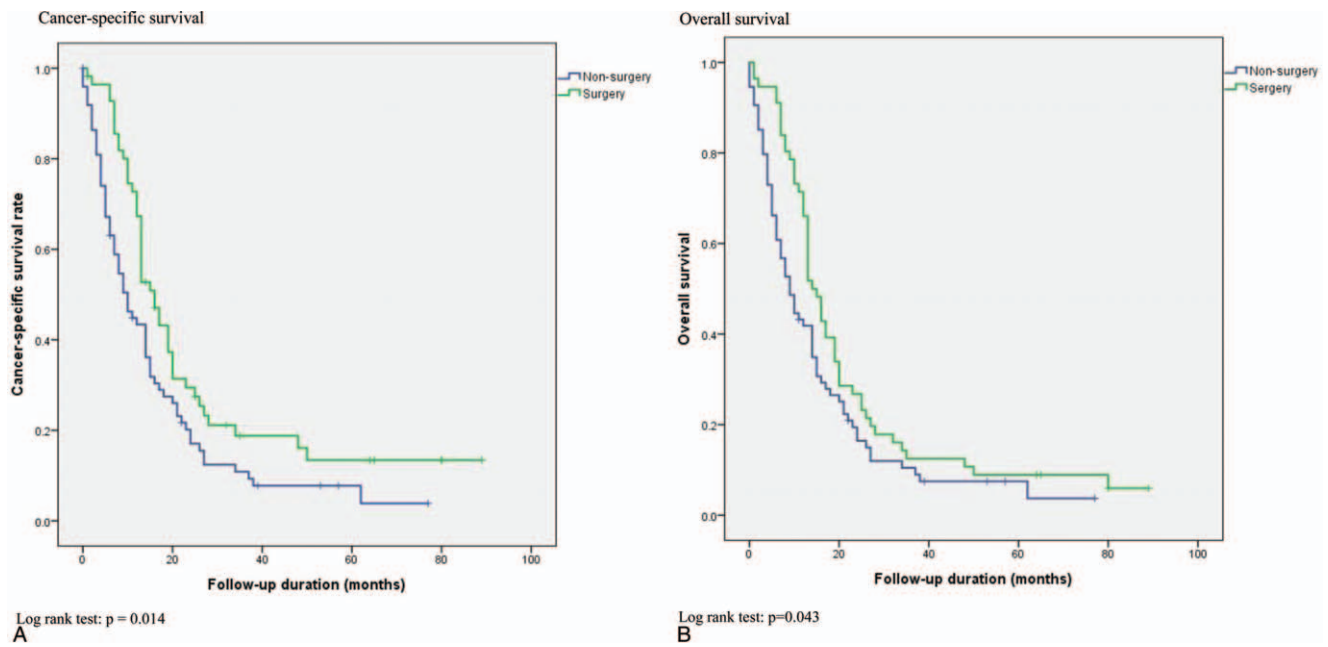
Figure 1. Kaplan-Meier curve of overall survival rates and cancer-specific survival in patients who received extirpative surgery versus systemic chemotherapy for metastatic urothelial carcinoma.

Table 4

Univariate and multivariate analysis of factors associated with cancer-specific survival.

Variables	Univariate analysis		Multivariate analysis	
	HR (95% CI)	P	HR (95% CI)	P
Sex		.579		
Male	1 (Ref)			
Female	1.154 (0.696–1.913)			
Age	1.006 (0.985–1.026)	.593		
BMI	0.942 (0.887–1.000)	.049	0.951 (0.892–1.013)	.116
ECOG		<.001		.001
≤1	1 (Ref)		1 (Ref)	
≥2	2.164 (1.438–3.256)		2.001 (1.313–3.050)	
Smoking		.63		
Nonsmoker	1 (Ref)			
Current or former smoker	1.098 (0.750–1.608)			
Clinical T stage		.273		
≤cT2	1 (Ref)			
≥cT3	0.754 (0.454–1.250)			
Clinical N stage		.242		
N0	1 (Ref)			
≥cN1	0.766 (0.491–1.197)			
Extirpative surgery		.017		.039
No	1 (Ref)		1 (Ref)	
Yes	0.630 (0.430–0.921)		0.663 (0.449–0.980)	
LN involved		.802		
No	1 (Ref)			
Yes	0.953 (0.656–1.385)			
Lung involved		.582		
No	1 (Ref)			
Yes	1.113 (0.760–1.632)			
Bone involved		.452		
No	1 (Ref)			
Yes	0.862 (0.584–1.270)			
Liver involved		<.001		.009
No	1 (Ref)		1 (Ref)	

Table 4

(continued).

Variables	Univariate analysis		Multivariate analysis	
	HR (95% CI)	P	HR (95% CI)	P
Yes	2.824 (1.619–4.923)		2.147 (1.210–3.807)	
Visceral involved		.894		
No	1 (Ref)			
Yes	0.972 (0.639–1.479)			
Tumor variant		.066		
No	1 (Ref)			
Yes	1.725 (0.964–3.086)			

BMI = body mass index, CI = confidential interval, ECOG = Eastern Cooperative Oncology Group, HR = hazard ratio, LN = lymph node.

Table 5

Univariate and multivariate analysis of factors associated with overall survival.

Variables	Univariate analysis		Multivariate analysis	
	HR (95% CI)	P	HR (95% CI)	P
Sex		.579		
Male	1 (Ref)			
Female	1.154 (0.696–1.913)			
Age	1.009 (0.989–1.030)	.359		
BMI	0.939 (0.886–0.994)	.032	0.952 (0.897–1.011)	.109
ECOG		<.001		<.001
≤1	1 (Ref)		1 (Ref)	
≥2	2.304 (1.556–3.412)		2.129 (1.423–3.185)	
Smoking		.534		
Nonsmoker	1 (Ref)			
Current or former smoker	1.124 (0.778–1.624)			
Clinical T stage		.493		
≤cT2	1 (Ref)			
≥cT3	0.839 (0.507–1.387)			
Clinical N stage		.365		
N0	1 (Ref)			
≥cN1	1.215 (0.798–1.849)			
Extirpative surgery		.05		.093
No	1 (Ref)		1 (Ref)	
Yes	0.694 (0.482–0.999)		0.723 (0.500–1.055)	
LN involved		.549		
No	1 (Ref)			
Yes	0.895 (0.623–1.286)			
Lung involved		.391		
No	1 (Ref)			
Yes	1.174 (0.814–1.692)			
Bone involved		.562		
No	1 (Ref)			
Yes	0.896 (0.617–1.300)			
Liver involved		.001		.008
No	1 (Ref)		1 (Ref)	
Yes	2.632 (1.513–4.577)		2.161 (1.227–3.807)	
Visceral involved		.915		
No	1 (Ref)			
Yes	1.023 (0.679–1.541)			
Tumor variant		.116		
No	1 (Ref)			
Yes	1.591 (0.892–2.838)			

BMI = body mass index, CI = confidential interval, ECOG = Eastern Cooperative Oncology Group, HR = hazard ratio, LN = lymph node.

However, there are not many studies about effects of LT on primary tumors in patients with metastatic UC. Recently, Seisen et al[16] reported the outcome of high-intensity LT (radical cystectomy or radiotherapy with >50 Gy) on the bladder in patients with metastatic BCa. The study population and clinical information were collected from the National Cancer Database (NCDB) registry, and inverse probability of treatment weighting was used for balancing covariates between 2 groups. The results

suggest that the median OS was much longer in the high-intensity LT group than the conservative LT group (14.92 vs 9.95 months, respectively; $P < .001$). Multivariate analysis also demonstrated high-intensity LT was associated with better OS (HR = 0.56, $P < .001$). Given the non-negligible morbidity associated with high-intensity LT, Vetterlein et al[17] tried to identify patients who might benefit the most from this treatment. Using the same NCDB registry, they showed that high-intensity LT provides an OS benefit, regardless of patient and tumor characteristics, in patients with metastatic, histologically pure UC of the bladder. Using the Japanese Urologic Association database registry, Inokuchi et al[24] reported the survival benefit of multimodal treatment in patients with metastatic UTUC. The group that underwent nephroureterectomy with chemotherapy had a significantly longer median OS than the groups that had supportive care, surgery alone, or chemotherapy alone (25.8 months vs 4.3 months vs 7.3 months vs 3.1 months, respectively; $P < .001$). The Cox proportional hazards regression model results in the Inokuchi et al's study also showed that multimodal treatment was associated with better prognosis than supportive care, chemotherapy alone, or surgery alone (HR = 0.32, $P = .001$). These results suggest that LT may improve survival in patients with metastatic UTUC. However, because patients who received supportive care alone were included in the comparison groups, it is difficult to conclusively assess the role of LT.

In our study, Kaplan-Meier curve results show that patients who underwent surgery for primary tumor had better OS. However, unlike the studies mentioned above, multivariate analysis demonstrated that surgery was not a significant predictor of OS. Rather, our study results suggest that surgery might improve CSS in patients with metastatic UC. And our results suggest that radical cystectomy and nephroureterectomy can be feasible for patients with metastatic UC, because not only perioperative outcomes including operative time, estimated blood loss, and transfusion rate but also postoperative complication rate of our study were similar to those previously reported for radical cystectomy or nephroureterectomy for standard indications in the previous study.[25,26]

Moreover, we investigated whether surgery for primary tumor affects the incidence of urinary tract complications and showed that the surgery group had a lower rate of urinary tract complications that required surgical intervention during follow-up. In the non-surgery group, 27.0% of the patients had to receive surgical intervention owing to urinary tract complications, whereas only 1.7% of patients in the surgery group underwent percutaneous nephrostomy owing to ureteral obstruction.

Previous studies concerned with oncologic outcome or prognostic factors of metastatic UC reported visceral metastasis as a significant predictor for survival. Bajorin et al[20] reported the median survival of patients with visceral metastasis was 11.1 months and without visceral metastasis was 22.3 months ($P = .0001$). They also showed that liver (9.87 vs 15.45 months, $P = .0001$) or lung metastasis (11.4 vs 15.6 months, $P = .024$) was related with poorer OS. Taguchi et al[27] also reported visceral metastasis was associated with poorer OS (HR = 1.424, 95% CI = 1.027–1.981, $P = .034$). However, our study showed only liver metastasis was associated with poorer CSS and OS. Involvement of distant LN, bone, and visceral organs (including liver, lung, and adrenal gland) did not affect either CSS or OS. Previous studies included patients with regional LN metastasis only (N+M0); thus, patients without distant metastasis were included as a comparison target of patients with visceral metastasis. However, our study excluded regional LN involvement without distant metastasis, and this difference appears to have produced different results.

Our study has some limitations. First, it is retrospective study from a single institution, and selection bias may be reflected in our results. Furthermore, we cannot control clinical variables that could affect survival, such as sex, age, BMI, smoking status, clinical TNM stage, and metastatic lesions. Especially, factors such as ECOG and liver metastasis, which seem to be associated with oncologic outcome, showed significant differences between the 2 groups. So, we tried to adjust significant heterogeneity using propensity score matching, but we couldn't. Because the number of patients included in our study was too small, and many patients were excluded from matching, matched cohort did not seem to reflect the characteristics of the entire cohort. If we included patients with only regional LN without distant metastasis or who had progressed to metastatic UC from initially localized UC, more patients would have been included in our study. However, there may be different tumor features between de novo metastatic disease and disease progressed to metastatic status compared with initially localized UC. Hence, our setting seems to be more homogeneous in the characteristics of the patient group. And previous studies have included not only radical cystectomy but also radiotherapy >50 Gy in high-intensity LT for metastatic BCa.[16,17] So, it is needed to evaluate whether radiotherapy can improve survival outcome in further study. There are other limitations in the analysis of complications. We found surgery for primary tumor may reduce the probability of urinary tract complications during follow-up. However, we did not evaluate the inconvenience associated with surgery. Some complications after radical cystectomy may be life-threatening, and 1 study reported that the 30-day mortality after radical cystectomy was 1.5%.[28] Moreover, radical cystectomy should be performed with diversion of the urinary tract. Ileal conduit urinary diversion or ureterocutaneostomy also can be factors associated with poor quality of life (QOL). Therefore, there should be further studies evaluating effect of surgery for primary tumor on QOL using questionnaires like the Functional Assessment of Cancer Therapy: Bladder Cancer, among others.[29,30]

Our results suggest that extirpative surgery for primary tumor in metastatic UC is feasible, and it may improve CSS and prevent urinary tract complications owing to disease progression and reduce probability for surgical intervention. Large, prospective, multicenter studies are needed to confirm these findings.

Author contributions

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