Original Article

Efficacy of cytoreductive surgery for metastatic upper tract urothelial carcinoma: a Surveillance, Epidemiology and End Results (SEER) study of 508 patients

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Background: Cisplatin-based combination chemotherapy alone is currently considered the standard of care for patients with metastatic upper tract urothelial carcinoma (mUTUC). However, less research has been done on the efficacy of other combinations. In this study, we explored the role of cytoreductive surgery in patients with mUTUC receiving different types of systemic therapy.

Methods: Data from 9,436 anonymized records were abstracted from the Surveillance, Epidemiology, and End Results (SEER) database between 2008–2018. Of these, 508 individuals received systemic therapy subsequent to being diagnosed with mUTUC. These patients had all been treated with systemic therapies such as chemotherapy and/or radiotherapy. Patients were stratified into either a non-surgical or surgical group based on cytoreductive surgery status before systemic therapeutics commenced. Kaplan-Meier curves were used to compare overall survival (OS) and cancer-specific survival (CSS). Cox's proportional hazard models were then used to analyze prognostic factors related to OS and CSS.

Results: Of the 508 cases, 36.8% (n=187) had received cytoreductive surgery with systemic treatments. The remaining 63.2% (n=321) received either chemotherapy and/or radiotherapy alone. Kaplan-Meier curves showed that 11.6% had 3-year OS [95% confidential interval (CI): 7.1–17.3] for cytoreductive surgery with systemic treatment and 4.9% (95% CI: 2.7–8.0) for systemic treatment alone (P=0.001). The 3-year CSS was 14.9% for cytoreductive surgery plus systemic treatment (95% CI: 9.4–21.7%) and 6.0% (95% CI: 3.4–9.8%) for systemic treatments alone (P=0.003). Under multivariate regression analysis, primary ureter site OS had a hazard ratio (HR) of 0.74 (95% CI: 0.58–0.95, P=0.02) and a CSS HR of 0.72 (95% CI: 0.56–0.94, P=0.01). The cytoreductive surgery OS HR was 0.79 (95% CI: 0.65–0.95, P=0.02) and the CSS HR was 0.75 (95% CI: 0.61–0.92, P=0.006). Additionally, chemotherapy had an OS HR of 0.46 (95% CI: 0.33–0.0.65, P<0.001) and a CSS HR of 0.44 (95% CI: 0.31–0.63, P<0.001). Bones and liver metastases were also indicative of poorer prognosis. Validation was conducted through subgroup analysis which suggested cytoreductive surgery was effective only for patients who received chemotherapy or combined chemo-radiotherapy but not for radiotherapy alone.

Conclusions: Cytoreductive surgery provided significantly increased OS and CSS for mUTUC patients who received chemotherapy or combined chemo-radiotherapy in this study. In addition, the primary tumor and metastatic sites were shown to be related to improved patient survival although this was a small and relatively homogeneous cohort of study, sample therefore, further research is required.

Keywords: Cytoreductive surgery; systemic treatment; metastatic upper tract urothelial carcinoma (mUTUC); overall survival (OS); cancer-specific survival (CSS)

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Introduction

Background

Approximately 10% of all patients with upper tract urothelial carcinoma (UTUC) present with extra-regional lymph nodes and/or other distant site metastases (1). This can vary substantially according to both demographics and clinical characteristics (2). Unfortunately, prognosis for these individuals is poor, with 3-year overall survival (OS) rates for metastatic upper tract urothelial carcinoma (mUTUC) not exceeding 10% (3). Besides, there are also differences in relation to treatment combinations. For example, Seisen *et al.*'s study based on the National Cancer Database showed that the 3-year OS of chemotherapy combined with radical nephroureterectomy was better than chemotherapy alone, with rates of 16.2% and 6.4%, respectively (4). Conversely, Necchi *et al.*'s study suggested that systemic chemotherapy after radical nephrectomy did not increase survival in patients with UTUC (5).

Rationale and knowledge gap

It remains unclear whether radiotherapy alone or in combination with other treatment modalities has a positive impact on prognosis for patients with UTUC (6). We do not yet know enough about treatment combinations and we do not yet know which patient groups will respond best to which combination and dosing, timing and other factors. Cisplatin-based combination chemotherapy alone is currently considered the standard of care for otherwise healthy patients with mUTUC (7). However, the metastatic tumor treatment paradigm is evolving and increasing evidence suggests there are benefits to controlling the primary focus, specifically for metastatic urothelial carcinoma (8). However, such tumors are relatively rare and so there are very few randomized controlled trials that compare treatment modalities. Indeed, there is very little evidence available or even data related to cytoreductive surgery for mUTUC. A recent study by Yoshida *et al.* suggested cytoreductive surgery outcomes improve when supplemented with chemotherapy although this was only preliminary research that requires further investigation (9).

Highlight box

Key findings

- Cytoreductive surgery provided significantly increased overall survival (OS) and cancer-specific survival (CSS) for metastatic upper tract urothelial carcinoma (mUTUC) patients who received chemotherapy or combined chemo-radiotherapy in this study.

What is known and what is new?

- Cisplatin-based combination chemotherapy alone is currently considered the standard of care for otherwise healthy patients with mUTUC. However, less research has been done on the efficacy of other combinations.
- In this study, we compared different treatment combinations of mUTUC patients based on data from the Surveillance, Epidemiology, and End Results (SEER) database.

What is the implication, and what should change now?

- The indication of cytoreductive surgery in mUTUC patients needs to be carefully. determined.

Objective

The Surveillance, Epidemiology, and End Results (SEER) database is a publicly available national data source developed in the US. Data of the SEER database are collected through local registries in 18+ US states. The purpose of the SEER database is to record time trends, pathologic evidence and treatment data as well as demographics and socio-economics and other factors. This data source makes it possible to analyse anonymized patient data to identify trends in primary data, which is especially useful for low prevalence diseases such as mUTUC. The objective of this study was to explore SEER data to understand the impact of cytoreductive surgery on OS and cancer-specific survival (CSS) for mUTUC patients who received systemic treatments. We present this article in accordance with the STROBE reporting checklist (available at https://tau.amegroups.com/article/view/10.21037/tau-23-619/rc).

Methods

Population

We extracted pertinent data from the SEER database in November 2020. The sample identified was of those diagnosed and treated between 2008–2018. Inclusion criteria were as follows: (I) primary tumor was identified using the International Classification of Diseases-O-3 (ICD-O-3) codes C64.9, C65.9; (II) initial primary tumor was confirmed to be urothelial carcinoma of the renal pelvis or ureter, and (III) histology was microscopically confirmed. Patients were excluded if metastasis, survival months, and vital status were unknown, and when the tumor was considered a secondary lesion. The main reason for the censoring of survival data was that some patients had not reached the clinical outcome at the data cutoff point. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013).

Description of covariates

Factor analysis included age, sex, ethnic origin, primary tumor sites, clinical T stage [American Joint Committee on Cancer (AJCC), 7th edition, 2010], clinical N stage (AJCC, 7th edition, 2010), radiotherapy, chemotherapy, surgery and metastatic sites (bone, liver, brain and lung).

Statistical analysis

Kaplan-Meier survival curves were calculated and compared using the log-rank test. Univariate analyses were used to assess associations between potential prognostic factors, i.e., age, gender, ethnic origin, primary site, tumor stage, cytoreductive surgery, systemic treatment regimen, metastatic site and survival. A standard Chi-squared test was used for categorical variables and an unpaired Student's *t* test was used to analyze outcomes in relation to age. Significant variables under univariate analyses were entered into a multivariate analysis (Cox stepwise-regression). P-values less than 0.05 were considered significant. All tests were conducted with SPSS (version 26.0).

Results

Patient's characteristics

Data for 9,436 anonymized patients were enrolled from the SEER database, of whom 508 individuals received systemic therapy subsequent to being diagnosed with mUTUC. All the histologic types of the patients included were transitional cell carcinoma. The median age of this sample was 67 years. There were 38.8% (n=197) were women and 84.3% (n=428) were Caucasian. All patients had received systemic treatment (either chemotherapy and/or radiotherapy) based on condition specifics.

Table 1 compares patient characteristics and clinical features of those who received cytoreductive surgery (n=187) and the population who did not receive cytoreductive surgery (n=321). Of the patients who underwent surgery, 142 had nephroureterectomy and 45 had local tumor resection. Compared to patients who did not receive cytoreductive surgery, patients with cytoreductive surgery had higher clinical T stages (P<0.001). There were no significant differences in relation to age, sex, ethnic origin, primary tumor sites, N stages, chemotherapy, radiotherapy, or metastatic sites between the groups, indicating these two groups were comparable.

Survival analysis based on cytoreductive surgery

The median follow-up was 8.0 months (interquartile range, 4.0–14.0 months). By 2018, approximately 88.4% (n=449) patients had died. Among these patients, 409 died as a result of developing UTUCs and 40 of other causes.

Kaplan-Meier curves (*Figure 1*) highlighted a 3-year OS of 11.6% [95% confidence interval (CI): 7.1–17.3%] for cytoreductive surgery plus systemic treatment and 4.9% (95% CI: 2.7–8.0%) for those who received systemic treatment alone (P=0.001). The 3-year CSS was 14.9% (95% CI: 9.4–21.7%) for cytoreductive surgery plus systemic treatment and 6.0% (95% CI: 3.4–9.8%) for systemic treatment alone (P=0.003).

Under Cox's regression analysis (*Table 2*), cytoreductive surgery was associated with a significant OS (HR 0.79, 95% CI: 0.65–0.95; P=0.02) and CSS (HR 0.75, 95% CI: 0.61–0.92; P=0.006) benefit. Similar results were observed for patients with primary ureter site (OS HR 0.74, 95% CI: 0.58–0.95, P=0.02; CSS HR 0.72, 95% CI: 0.56–0.94, P=0.01). This was consistent for chemotherapy which had an OS HR of 0.46 (95% CI: 0.33–0.65, P<0.001) and a CSS HR of 0.44 (95% CI: 0.31–0.63, P<0.001). In addition, metastatic bone sites (CSS HR 1.31, 95% CI: 1.07–1.62, P=0.01) and liver (OS HR 1.46, 95% CI: 1.21–1.78, P<0.001; CSS HR 1.46, 95% CI: 1.19–1.79, P<0.001) had poor survival.

Subgroup analysis based on different systemic treatment

Due to significant differences in radiotherapy under both univariate analysis and multivariate analysis, we further

Table 1 Baseline characteristics of patients who received systemic treatment plus cytoreductive surgery versus systemic treatment alone for metastatic upper tract urothelial carcinoma study populations from the SEER data base, 2008–2018

Characters	Overall (n=508)	Cytoreductive surgery (n=187)	Non-cytoreductive surgery (n=321)	P value
Age (years)	69 [61–72]	69 [62–75]	69 [61–77]	0.97
Sex				0.78
Male	311 (61.2)	116 (62.0)	195 (60.7)	
Female	197 (38.8)	71 (38.0)	126 (39.3)	
Race				0.94
White	428 (84.3)	156 (83.4)	272 (84.7)	
Black	35 (6.9)	13 (7.0)	22 (6.9)	
Others	45 (8.8)	18 (9.6)	27 (8.4)	
Primary site				0.90
Renal pelvic	417 (82.1)	153 (81.8)	264 (82.2)	
Ureter	91 (17.9)	34 (18.2)	57 (17.8)	
T				<0.001
T1	111 (21.9)	9 (4.8)	102 (31.8)	
T2	40 (7.9)	6 (3.2)	34 (10.6)	
T3	183 (36.0)	95 (50.8)	88 (27.4)	
T4	174 (34.3)	77 (41.2)	97 (30.2)	
N				0.60
N0	172 (33.9)	66 (35.3)	106 (33.0)	
N1–3	336 (66.1)	121 (64.7)	215 (67.0)	
Chemotherapy				0.24
No	66 (13.0)	20 (10.7)	46 (14.3)	
Yes	442 (87.0)	167 (89.3)	275 (85.7)	
Radiotherapy				0.18
No	354 (69.7)	137 (73.3)	217 (67.6)	
Yes	154 (30.3)	50 (26.7)	104 (32.4)	
Bone metastases				0.25
No	271 (53.3)	106 (56.7)	165 (51.4)	
Yes	237 (46.7)	81 (43.3)	156 (48.6)	
Brain metastases				0.15
No	489 (96.3)	183 (97.9)	306 (95.3)	
Yes	19 (3.7)	4 (2.1)	15 (4.7)	
Liver metastases				0.09
No	418 (62.6)	126 (67.4)	192 (59.8)	
Yes	190 (37.4)	61 (32.6)	129 (40.2)	

Table 1 (*continued*)

Table 1 (*continued*)

Characters	Overall (n=508)	Cytoreductive surgery (n=187)	Non-cytoreductive surgery (n=321)	P value
Lung metastases				0.67
No	210 (41.3)	75 (40.1)	135 (42.1)	
Yes	298 (58.7)	112 (59.9)	186 (57.9)	
Distant lymph node metastases				0.60
No	460 (90.6)	171 (91.4)	289 (90.0)	
Yes	48 (9.4)	16 (8.6)	32 (10.0)	
Other metastases				0.10
No	484 (95.3)	182 (97.3)	302 (94.1)	
Yes	24 (4.7)	5 (2.7)	19 (5.9)	

Continuous variables are reported as median [interquartile range] and categorical variables as number (%). SEER, Surveillance, Epidemiology, and End Results.

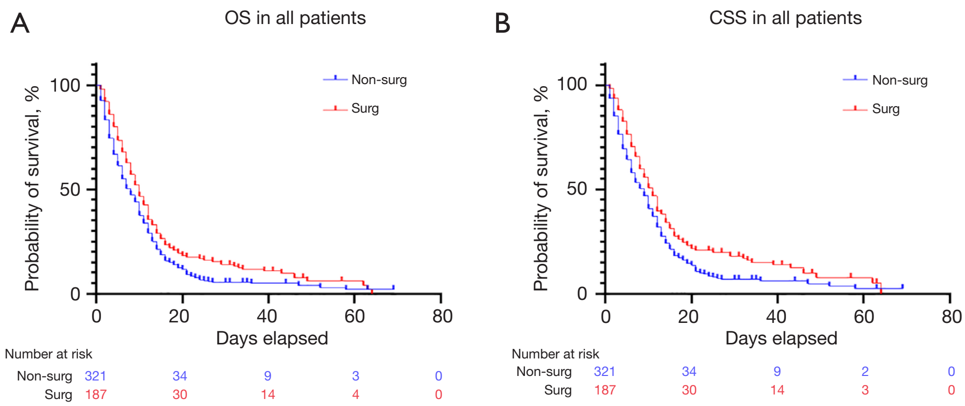

Figure 1 Kaplan-Meier analysis of OS (A) and CSS (B) among patients who received systemic treatment plus cytoreductive surgery versus systemic treatment alone for metastatic upper tract urothelial carcinoma. OS, overall survival; CSS, cancer-specific survival.

Table 2 Univariate and multivariate Cox regression models predicting overall survival and cancer-specific survival of metastatic upper tract urothelial carcinoma after cytoreductive surgery

Characters	Overall survival				Cancer-specific survival			
	Univariate analysis		Multivariate analysis		Univariate analysis		Multivariate analysis	
	HR (95% CI)	P	HR (95% CI)	P	HR (95% CI)	P	HR (95% CI)	P
Age (years)	1.00 (0.99–1.01)	0.50			1.00 (0.99–1.01)	0.75		
Sex								
Male	Ref				Ref			
Female	1.10 (0.91–1.33)	0.31			1.12 (0.92–1.37)	0.26		
Race		0.13				0.08		
White	Ref				Ref			
Black	1.46 (1.01–2.11)	0.042			1.58 (1.06–2.35)	0.02		
Others	0.74 (0.26–2.13)	0.58			0.65 (0.19–2.21)	0.49		

Table 2 (*continued*)

Table 2 (*continued*)

Characters	Overall survival				Cancer-specific survival			
	Univariate analysis		Multivariate analysis		Univariate analysis		Multivariate analysis	
	HR (95% CI)	P	HR (95% CI)	P	HR (95% CI)	P	HR (95% CI)	P
Primary site								
Pelvic	Ref				Ref			
Ureter	0.76 (0.60–0.976)	0.03	0.74 (0.58–0.95)	0.02	0.75 (0.58–0.97)	0.03	0.72 (0.56–0.94)	0.01
T		0.10				0.19		
T1	Ref				Ref			
T2	0.78 (0.60–1.00)	0.05			0.78 (0.59–1.02)	0.07		
T3	0.95 (0.66–1.35)	0.76			0.98 (0.68–1.42)	0.91		
T4	0.78 (0.63–0.97)	0.03			0.82 (0.65–1.03)	0.09		
N								
N0	Ref				Ref			
N1–3	0.99 (0.81–1.20)	0.92			0.99 (0.81–1.22)	0.96		
Cytoreductive surgery								
No	Ref				Ref			
Yes	0.76 (0.62–0.92)	0.005	0.79 (0.65–0.95)	0.015	0.73 (0.59–0.89)	0.002	0.75 (0.61–0.92)	0.006
Chemotherapy								
No	Ref				Ref			
Yes	0.45 (0.34–0.59)	<0.001	0.46 (0.33–0.65)	<0.001	0.43 (0.32–0.57)	<0.001	0.44 (0.31–0.63)	<0.001
Radiotherapy								
No	Ref				Ref			
Yes	1.32 (1.08–1.62)	0.006	0.94 (0.77–1.32)	0.94	1.35 (1.09–1.67)	0.005	0.99 (0.75–1.31)	0.93
Bone metastases								
No	Ref				Ref			
Yes	1.21 (1.01–1.46)	0.043	1.22 (1.00–1.49)	0.054	1.30 (1.07–1.58)	0.008	1.31 (1.07–1.62)	0.01
Brain metastases								
No	Ref				Ref			
Yes	1.78 (1.11–2.86)	0.02	1.18 (0.71–1.96)	0.52	1.74 (1.05–2.88)	0.03	1.16 (0.68–1.99)	0.59
Liver metastases								
No	Ref				Ref			
Yes	1.44 (1.19–1.74)	<0.001	1.46 (1.21–1.78)	<0.001	1.43 (1.17–1.75)	<0.001	1.46 (1.19–1.79)	<0.001
Lung metastases								
No	Ref				Ref			
Yes	0.95 (0.79–1.14)	0.57			0.92 (0.76–1.12)	0.42		
Distant lymph node metastases								
No	Ref				Ref			
Yes	0.99 (0.69–1.43)	0.98			0.99 (0.68–1.44)	0.96		
Other metastases								
No	Ref				Ref			
Yes	0.81 (0.50–1.29)	0.37			0.84 (0.51–1.36)	0.47		

HR, hazard ratio; CI, confidence interval.

Table 3 Patients receiving cytoreductive surgery in different systemic therapy groups

Systemic treatment	Overall (n=508)	Cytoreductive surgery (n=187)	Non-cytoreductive surgery (n=321)
Chemotherapy alone	354 (69.7)	137 (73.3)	217 (67.6)
Radiotherapy alone	66 (13.0)	20 (10.7)	46 (14.3)
Combined chemoradiotherapy	88 (17.3)	30 (16.0)	58 (18.1)

Categorical variables are reported as number (%).

explored the role of different systemic treatments through subgroup analyses. Among all cases, 69.7% (n=354) patients received chemotherapy alone as systemic treatment, 13.0% (n=66) received radiotherapy alone as systemic treatment, and 17.3% (n=88) received combined chemoradiotherapy (*Table 3*).

In patients who received radiotherapy alone, cytoreductive surgery had no significant effect on OS [surgery *vs.* non-surgery: 6.5 (95% CI: 4.2–8.7) *vs.* 5.8 (95% CI: 3.6–8.0) months, P=0.40] or CSS [surgery *vs.* non-surgery: 6.8 (95% CI: 4.4–9.1) *vs.* 6.2 (95% CI: 3.8–8.7) months, P=0.45]. Whereas, in patients treated with chemotherapy, OS of surgery *vs.* non-surgery were 15.8 months (95% CI: 12.8–18.7) *vs.* 12.0 months (95% CI: 10.2–12.8), P=0.046. For CSS, surgery *vs.* non-surgery were 18.1 months (95% CI: 14.6–21.6) *vs.* 12.9 months (95% CI: 10.9–14.9), P=0.02. Combined chemoradiotherapy had an OS for surgery *vs.* non-surgery of 18.5 months (95% CI: 11.4–25.7) *vs.* 10.5 months (95% CI: 7.5–13.5), P=0.03. CSS for surgery *vs.* non-surgery were significantly different at 19.2 months (95% CI: 11.9–26.4) *vs.* 11.9 months (95% CI: 7.8–16.0), P=0.049. Cytoreductive surgery also had a significant benefit on both OS and CSS (*Figure 2*).

Discussion

Upper urinary tract urothelial carcinoma is a relatively rare disease, accounting for 5% to 10% of all urothelial malignancies (10). However, OS for patients with UTUC is generally lower than for those with bladder cancer. The reason is that most (>60%) of UTUC patients had early invasion at diagnosis, which only occurs in 15–25% of bladder urothelial carcinoma (BUC) patients (11). Worse still, approximately 10% of patients with UTUC present with locally advanced cancer or metastasis at initial diagnosis, and the prognosis is poor, with a 3-year OS lower than 10% (1). Therefore, greater consideration must be given to addressing the treatment of metastatic UTUC patients.

This investigation utilized data from the SEER database and analyzed information collected from 508 patients. Of this group, 36.8% (187/508) underwent cytoreductive surgery while 63.2% (321/508) received systemic treatment alone. In the queue, the median survival was only 8.0 months, 88.4% patients (449/508) had succumbed by 2018, which is consistent with the known ominous prognosis of mUTUC (1). Through survival analysis and impact factor analysis, we found that different combinations of cytoreductive surgery and systemic therapy had a significant impact on the prognosis of patients. Furthermore, we also obtained evidence of the effect of the primary site and metastatic site of the tumor on the prognosis.

Among patients who received systemic therapy, those who also received cytoreductive surgery had higher clinical T stages but had better survival, and cytoreductive surgery was associated with survival in multivariate analysis. There is a dearth of literature detailing the usage of cytoreductive surgery for metastatic urologic tumors. Although the CARMENA trial established that systemic therapy was noninferior to cytoreductive nephrectomy, prior to this clinical study, surgery combined with cytokine therapy was commonly accepted as standard therapy for metastatic renal cell carcinoma (12,13). In bladder cancer literature, local therapy has been demonstrated to provide survival benefits when compared to patients treated with chemotherapy only (14,15). A National Cancer Database study reported a survival benefit for surgery in 173 patients with cM1 UTUC, regardless of chemotherapy administration (8). Our study, with a larger sample size than previous studies, cautiously supports the integration of consolidative surgery along with perioperative systemic therapy for UTUC that may better define the role of surgery in advanced UTUC.

As has been reported in previous studies, advanced UTUC can be responsive to systemic chemotherapy. For decades, cisplatin-based regimens have been known as most the active first-line agents (16). MVAC became the primary regimen for metastatic UTUC after exhibiting a survival benefit with an improved median survival of 13 months,

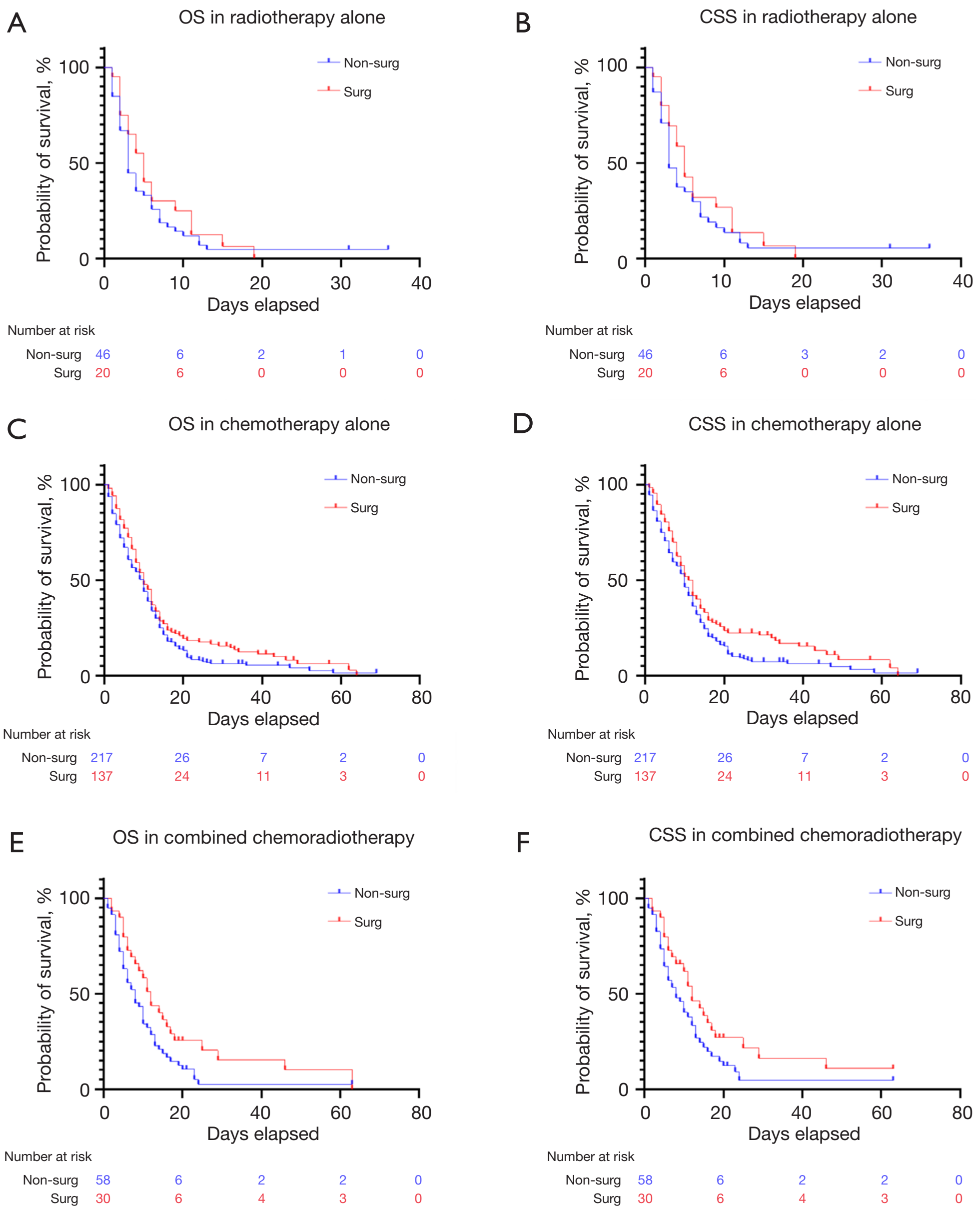

Figure 2 Kaplan-Meier analysis of overall survival and cancer-specific survival among patients in different systemic therapy groups (A,B: radiotherapy alone; C,D: chemotherapy alone; E,F: combined chemoradiotherapy). OS, overall survival; CSS, cancer-specific survival.

despite significant toxicity (17). Recently, combination gemcitabine-cisplatin (GC) therapy has been indicated to be better tolerated than the combination therapy of methotrexate, vinblastine, doxorubicin, and cisplatin (MVAC) with similar efficacy. One trial uncovered similar OS (13.8 months with GC *vs.* 14.8 months with MVAC) with patients who received GC experiencing fewer toxic side effects (18). The use of cisplatin-based chemotherapy is widely considered in patients with estimated glomerular filtration rate (eGFR) >45 mL/min. Furthermore, with the emergence of immune checkpoint inhibitors in primary and maintenance settings, there may exist an opportunity to further characterize the role of cytoreductive surgery for surgically fit patients requiring symptom palliation (such as recalcitrant pain, hematuria, or collecting system obstruction) (16), which holds the promise of enhancing patient quality of life and prolonging survival.

It is crucial to understand that in both OS and CSS analyses, radiotherapy showed a correlation with survival in univariate regression but not in multivariate regression. This may be due to the fact that radiotherapy is a local treatment that can alleviate tumor-related symptoms and tumor growth rate, but it may not directly improve patient prognosis (12). Besides, the use of radiotherapy alone typically occurs in advanced patients who may not be eligible for surgical treatment. As a result, other negative factors caused by advanced tumors may outweigh the benefits of treatment, leading to poorer patient survival (6). However, a recent study conducted by Zhang *et al.* in 2021 suggested that radiotherapy can be beneficial to OS in UTUC patients, particularly in patients with N1/2/3 (19). Consequently, the efficacy of systemic radiotherapy alone and in combination with other treatment modalities necessitates further investigation.

We also examined the impact of cytoreductive surgery on the three groups of patients (chemotherapy alone, radiotherapy alone, and combined chemoradiotherapy) by subdividing the specific systemic therapy for each patient. The results revealed that cytoreductive surgery improved the survival outcomes of patients with chemotherapy alone or combined chemoradiotherapy, but did not have any survival benefits for patients with radiotherapy alone. The primary reason that cytoreductive surgery enhanced the prognosis of patients receiving chemotherapy was its ability to reduce the local tumor burden, resulting in a better response to chemotherapy (4,14). However, for patients with mUTUC, the lack of systemic treatment for the systemic tumor implies that radiotherapy alone or radiotherapy after cytoreductive surgery has no effect on the overall prognosis.

In addition, our cox regression analysis showed that the primary tumor site was associated with patient survival. Previous research has suggested that patients with renal pelvis urothelial carcinoma have better OS compared to patients with ureter urothelial carcinoma (20). This is attributed to the fact that the exogenous ureter is relatively thinner and has a higher possibility of tumor invasion into the peripheral lymphatic and vascular network (20). However, we found that once metastasis occurs, patients with ureter urothelial carcinoma tend to have a better prognosis. In our opinion, if renal pelvis urothelial carcinoma can penetrate the barrier of renal parenchyma and surrounding adipose tissue, it indicates an extremely advanced primary tumor, which is typically associated with a poorer prognosis.

Consistent with previous studies, our research found that lung metastasis was the most common, followed by bone and liver metastases. Brain metastasis is a relatively rare occurrence (21,22). While several retrospective studies have found that metastasis to specific organs such as the liver and bone may predict a poorer prognosis, most researchers agree that the number of metastatic organs, which reflects the overall tumor burden, is a stronger predictor of prognosis in mUTUC than the presence of visceral metastasis alone (22-24). Therefore, it is important to consider the extent of metastasis, along with other prognostic factors, when determining the optimal treatment approach for patients with mUTUC.

Our investigation had several limitations. Firstly, we lacked information regarding the treatment sequence, which limited our ability to fully assess the impact of these variables on patient outcomes. Secondly, we were unable to determine the specific types and number of cycles administered for systemic chemotherapy, as well as those who received radiotherapy in conjunction with or after chemotherapy, due to a lack of granularity in the SEER summary variable. Furthermore, since the SEER database did not provide further description of functional characteristics, we were unable to analyze the impact of complications and functional status on patient outcomes. These limitations highlight the need for more detailed and comprehensive data collection in future studies to better understand the factors that influence prognosis in patients with mUTUC.

Conclusions

In conclusion, our study found that fit patients with mUTUC who received cytoreductive surgery had improved OS and CSS. Although the observational study design introduces certain biases and limitations, our preliminary findings provide strong evidence for the potential benefits of aggressive local treatment of the primary tumor in metastatic urothelial carcinoma. Furthermore, our study identified important prognostic factors for mUTUC, including the number of metastatic organs and primary tumor site. These factors should be taken into account when designing effective treatment plans for patients with mUTUC. Overall, our results have important clinical implications and suggest that future randomized controlled trials should further investigate the potential benefits of aggressive local treatment in mUTUC.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://tau.amegroups.com/article/view/10.21037/tau-23-619/rc

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://tau.amegroups.com/article/view/10.21037/tau-23-619/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013).

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