

Original article

The comparison of oncologic outcomes between metastatic upper tract urothelial carcinoma and urothelial carcinoma of the bladder after cisplatin-based chemotherapy

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Abstract

Objective: To compare the oncologic outcomes and prognostic factors between metastatic upper tract urothelial carcinoma (UTUC) and UC of the bladder (UCB) after cisplatin-based chemotherapy.

Materials and methods: We retrospectively reviewed patients with metastatic UTUC and UCB after methotrexate/vinblastine/doxorubicin/cisplatin (MVAC) or gemcitabine/cisplatin chemotherapy between 1997 and 2014 at Kaohsiung Chang Gung Memorial Hospital. Progression-free survival (PFS) and overall survival (OS) were estimated by the Kaplan-Meier method. Univariate and multivariate analyses with Cox proportional hazard models were also performed to assess the effect of prognostic factors.

Results: Totally, 203 patients were enrolled into our study, including 120 patients with UTUC and 83 patients with UCB. For patients with UTUC, the median PFS was 7.3 months vs. 4.0 months ($P < 0.001$), and the median OS was 17.0 months vs. 10.5 months ($P < 0.001$) for MVAC and gemcitabine/cisplatin, respectively. For patients with UCB, the median PFS ($P = 0.35$) and OS ($P = 0.06$) of the 2 groups were insignificant. In multivariate analyses, number of metastatic sites was the identical prognostic factor for OS between UTUC (hazard ratio [HR] = 2.74; 95% CI: 1.63–4.62; $P < 0.001$) and UCB (HR = 3.12; 95% CI: 1.52–6.39; $P = 0.002$). Presence of liver metastasis (HR = 1.84; 95% CI: 1.05–2.23; $P = 0.03$) and MVAC chemotherapy (HR = 0.54; 95% CI: 0.35–0.83; $P < 0.001$) were significantly correlated to survival only for UTUC, not for UCB.

Conclusion: Our study suggests discordant oncologic outcomes and prognostic factors between metastatic UTUC and UCB after cisplatin-based chemotherapy. A prospective study is warranted to validate our results. © 2015 Elsevier Inc. All rights reserved.

Keywords: Metastatic upper tract urothelial carcinoma; Metastatic urothelial carcinoma of the bladder; Oncologic outcome; Prognostic factor

1. Introduction

Urothelial carcinoma (UC) is a malignant tumor that has become the fourth and eighth most common cancer in men and women, respectively, in the United States. Approximately 141,000 cases of UC were diagnosed in the United States in 2012 and 29,000 of those patients died from the disease [1]. For decades, a cisplatin-based regimen has been accepted as the optimal chemotherapy for UC [2]. Methotrexate/vinblastine/doxorubicin/cisplatin (MVAC) [3] and gemcitabine/cisplatin (GC) are 2 commonly used combination chemotherapy

regimens [4]. The MVAC regimen was developed at Memorial Sloan-Kettering Cancer Center in the 1980s. The response rate for UC was 72% in 121 cases of bidimensionally measurable diseases [5]. von der Maase et al. [4] demonstrated that GC provided a similar survival advantage as that of MVAC with a better safety profile and improved tolerability in UC of the bladder (UCB). The response rates of GC and MVAC were 49% and 46%, respectively. Therefore, GC was accepted to be the first-line chemotherapy for locally advanced or metastatic UCB, instead of MVAC.

Upper tract UC (UTUC) is a less common disease than UCB, accounting for only 5% to 10% of urothelial malignancies in Western countries [1]. Taiwan is an endemic area of “blackfoot disease” since the 1950s,

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contributing to more UTUC cases than in Western countries. The ratios of UC of the renal pelvis, ureter, and bladder in Taiwan were estimated to be 1:2.08:6.72 during 1983 to 1998 [6]. Current consensus on chemotherapy for UTUC was based on those for UCB. However, some studies suggested that patients with UTUC may have a different biology and outcome from those with UCB, despite sharing the same histology [7–11]. To date, a limited literature has focused on the response of chemotherapy for metastatic UTUC [12]. As there are no conclusive studies at present, the purpose of our study is to compare the oncologic outcomes and prognostic factors of metastatic UTUC and UCB after cisplatin-based chemotherapy.

2. Materials and methods

2.1. Patient population

This retrospective study was approved by the Institutional Review Board. Patients who were diagnosed to have metastatic UC and received MVAC or GC as first-line chemotherapy between 1997 and 2013 at Kaohsiung Chang Gung Memorial Hospital were enrolled. Tumor staging was determined according to the seventh edition of the American Joint Committee on Cancer/Union Internationale

Contre le Cancer TNM classification [13]. Multifocal UC was stratified according to the dominant tumor site. Renal function was presented by using the abbreviated Modification of Diet in the Renal Disease Study Equation (MDRD) [14].

2.2. Statistical analysis

The statistical end points were progression-free survival (PFS), overall survival (OS), and objective response rate (ORR). PFS was calculated as the duration from the starting date of chemotherapy to the date when the disease worsened or recurred. OS was calculated from the starting date of chemotherapy to the date of death or the last contact when the patients were still alive at the time of the follow-up visit. ORR was defined as the ratio of complete remission to partial response according to Response Evaluation Criteria in Solid Tumors (RECIST; version 1.1). Demographic and clinicopathologic characteristics were analyzed between both groups using the Pearson chi-square test. Kaplan-Meier curves with a log-rank test were used to estimate the PFS and OS. Multivariate analyses were conducted using Cox proportional hazard models for PFS and OS with “enter” selection to adjust for the effects of potential confounders. All statistical tests were 2 sided. *P*-values < 0.05 were considered to be statistically significant.

Table 1
Basic characteristics of metastatic urothelial carcinoma treated with systemic chemotherapy

	UTUC		<i>P</i> value	UCB		<i>P</i> value
	MVAC <i>n</i> = 61	GC <i>n</i> = 59		MVAC <i>n</i> = 28	GC <i>n</i> = 55	
Gender			0.17			0.06
Male	35 (57%)	41 (70%)		23 (82%)	34 (62%)	
Female	26 (43%)	18 (30%)		5 (18%)	21 (38%)	
Age			0.46			0.96
≤ 60	32 (53%)	27 (46%)		9 (32%)	18 (33%)	
> 60	29 (47%)	32 (54%)		19 (68%)	37 (67%)	
Performance status			0.47			0.5
0–1	45 (74%)	40 (68%)		20 (71%)	43 (78%)	
≥ 2	16 (26%)	19 (32%)		8 (29%)	12 (22%)	
Renal function			0.37			0.41
CCr ≥ 60	42 (69%)	36 (61%)		19 (68%)	42 (76%)	
CCr < 60	19 (31%)	23 (39%)		9 (32%)	13 (24%)	
Metastatic sites						
Lymph node metastasis	44 (72%)	42 (71%)	0.91	18 (64%)	42 (76%)	0.25
Lung metastasis	10 (16%)	14 (24%)	0.32	6 (21%)	6 (11%)	0.2
Liver metastasis	12 (20%)	17 (29%)	0.24	8 (29%)	8 (15%)	0.13
Bone metastasis	6 (10%)	10 (17%)	0.25	2 (7%)	6 (11%)	0.58
Number of disease sites			0.15			0.98
1	40 (66%)	31 (53%)		18 (64%)	36 (66%)	
≥ 2	21 (34%)	28 (48%)		10 (36%)	19 (35%)	
Second-line chemotherapy			0.95			0.19
No	41 (67%)	40 (68%)		20 (71%)	46 (84%)	
Yes	20 (33%)	19 (32%)		8 (29%)	9 (16%)	

CCr = creatinine clearance rate.

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