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Original article

Incidence, characteristics, treatment strategies, and oncologic outcomes of synchronous bilateral upper tract urothelial carcinoma in the Chinese population

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Abstract

Objectives: To investigate the incidence and treatment strategies for bilateral upper tract urothelial carcinoma (UTUC) and to compare the characteristic and oncologic outcomes of bilateral UTUC with those of unilateral tumors.

Methods and materials: The study included 892 consecutive patients with UTUC. Bilateral UTUC was defined as synchronous bilateral carcinoma on preoperative imaging before confirmation by pathology or positive urine cytology result plus direct visualization. Radical nephroureterectomy (RNU) or nephron-sparing surgery (NSS) or both were carried out.

Results: A total of 39 patients (4.37%) suffered from bilateral disease. Discordant histological grade of bilateral tumor was found in 39.3% cases. Bilateral tumors were associated with female sex ($P < 0.001$), preoperative renal insufficiency ($P < 0.001$), previous or concomitant bladder tumors ($P = 0.013$), lower tumor stages ($P = 0.020$), papillary architecture ($P = 0.001$), and smaller-sized tumors ($P = 0.020$). Patients with worse renal function ($P < 0.001$) or large-sized tumors ($P = 0.039$) tended to be treated with bilateral RNU. Most patients (67.6%) were treated with unilateral RNU plus unilateral NSS, with NSS being performed on tumors that only extended to the ureter ($P = 0.003$) and had a smaller size ($P = 0.005$). The median follow-up duration was 56 months. The 5-year cancer-specific survival and bladder recurrence-free survival rates were 81.2% and 64.5%, respectively, similar to those of unilateral tumors. Male sex (hazard ratio = 11.535) and higher tumor stage (hazard ratio = 3.386) were independent worse prognostic factors.

Conclusions: The prevalence of bilateral UTUC is rare. Female patients, patients with renal insufficiency, and those with bladder tumor tended to suffer from bilateral disease and were less likely to present with worse pathological outcomes in the Chinese population. The tumor characteristics and renal function were informative in treatment selection. The oncologic outcomes were similar to those in unilateral UTUC, and male sex and a higher tumor stage were poor prognostic factors for these patients.

Keywords: Bilateral; Chronic kidney disease (CKD); Sex; Nephron-sparing surgery (NSS); Radical nephroureterectomy (RNU); Upper tract urothelial carcinoma (UTUC)

1. Introduction

Upper tract urothelial carcinomas (UTUC) are uncommon and account for only 5% to 10% of urothelial carcinomas [1,2]. Synchronous bilateral UTUC is even rarer. A large Swedish study reported that only 1.6% of

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Table 1
Clinical and pathological characteristics of bilateral UTUC compared with unilateral tumors

	All	Presence of UTUC		Univariate analysis		Multivariate analysis		
		Unilateral	Bilateral	χ^2 or Z	P value	HR	95% CI	P value
Patients, no. (%)	892 (100)	853 (95.6)	39 (4.4)					
Preoperative characteristics								
Sex, no. (%)				11.926	<0.001*			
Male	400 (44.8)	393 (46.1)	7 (17.9)			3.534 (female vs. male)	1.466–8.523	0.005*
Female	492 (55.2)	460 (53.9)	32 (82.1)					
Age, no. (%), y				0.175	0.402			
<70	497 (55.7)	474 (55.6)	23 (59.0)			0.842 (≥70 vs. <70)	0.427–1.659	0.618
≥70	395 (44.3)	379 (44.4)	16 (41.0)					
Age, mean ± SD, y		66.59 ± 10.57	67.35 ± 7.34	−0.047	0.962			
Gross hematuria, no. (%)				0.121	0.448	0.991 (present vs. absent)	0.451–2.178	0.982
Absent	227 (25.4)	218 (25.6)	9 (23.1)					
Present	665 (74.6)	635 (74.4)	30 (76.9)					
Previous or concomitant BT, no. (%)				6.860	0.013*			
Absent	751 (84.2)	724 (84.9)	27 (69.2)			2.393 (present vs. absent)	1.139–5.026	0.021*
Present	141 (15.8)	129 (15.1)	12 (30.8)					
Preoperative renal function, no. (%)				18.879	<0.001*			
No CKD (eGFR ≥ 60)	388 (43.5)	379 (44.4)	9 (23.1)			5.192 (end-stage vs. no CKD)	1.909–14.120	0.001*
Moderate CKD (60 > eGFR ≥ 15)	441 (49.4)	420 (49.2)	21 (53.8)			2.477 (end-stage vs. moderate CKD)	1.039–5.904	0.041*
End-stage CKD (eGFR < 15)	63 (7.1)	54 (6.3)	9 (23.1)					
History of smoking, no. (%)				3.108	0.051			
Absent	728 (81.6)	692 (81.1)	36 (92.3)			0.721 (present vs. absent)	0.204–2.547	0.612
Present	164 (18.4)	161 (18.9)	3 (7.7)					
Urinary cytology, no. (%)				0.510	0.775			
Negative	201 (22.5)	194 (22.7)	7 (17.9)			1.277 (positive vs. negative)	0.511–3.195	0.601
Missing data	316 (35.4)	301 (35.3)	15 (38.5)			1.070 (positive vs. missing)	0.511–2.243	0.857
Positive	375 (42.0)	358 (42.0)	17 (43.6)					
Postoperative characteristics								
Architecture, no. (%)				8.319	0.001*			
Papillary	685 (76.8)	649 (76.1)	36 (92.3)					
Sessile	192 (21.5)	191 (22.4)	1 (2.6)					
Tumor stage, no. (%)[a]				7.777	0.020*			
Ta–T1	314 (35.2)	292 (34.2)	22 (56.4)					
T2	297 (33.3)	288 (33.8)	9 (23.1)					
T3–T4	273 (30.6)	265 (31.1)	8 (20.5)					
Lymph node status, no. (%)				1.076	0.584			
N0	96 (10.8)	90 (10.6)	6 (15.4)					
Nx	760 (85.2)	728 (85.3)	32 (82.1)					
N+	36 (4.0)	35 (4.1)	1 (2.6)					
Tumor grade, no. (%)[a]				0.666	0.717			
G1	27 (3.0)	25 (2.9)	2 (5.1)					
G2	505 (56.6)	484 (56.7)	21 (53.8)					
G3	358 (40.1)	342 (40.1)	16 (41.0)					
Tumor size, mean ± SD[a]		3.41 ± 2.22	2.54 ± 1.46	−2.323	0.020*			

eGFR = estimated glomerular filtration rate; HR = hazard ratio; SD = standard deviation.
*Statistically significant.
[a]The higher stage/grade and larger size of bilateral tumors were used for analysis.

UTUC were bilateral [3]. The only commonly accepted shared characteristic of these patients is their renal insufficiency [3–5], and proper treatment measures for bilateral UTUC remain to be elucidated.

Radical nephroureterectomy (RNU) with the resection of bladder cuff is the gold standard treatment for UTUC [6]; however, for patients with bilateral UTUC, the resection of both kidneys would lead to the total loss of renal function and inevitable permanent dialysis. Nephron-sparing surgery (NSS), such as segmental ureterectomy or endoscopic management, has been shown to provide a cancer-specific and overall survival (CSS and OS) equivalent to that of