



Original Article

Clinical and demographic characteristics among patients with urothelial carcinomas of the upper urinary tract and bladder in Taiwan

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Abstract

Background: Urothelial carcinoma (UC) is derived from the urothelium of the urinary tract, and includes cancers of the bladder, renal pelvis and ureter. The aim of this study was to investigate the clinical and demographic features among patients with bladder cancer and urothelial carcinoma of the upper urinary tract (UTUC) in Taiwan.

Methods: The present study recruited a total of 736 histopathologically confirmed UC cases, which consisted of 470 bladder cancer and 266 UTUC between September 1998 and December 2009. Clinical and demographic features were collected by an interview utilizing a structured questionnaire, and supplemented by medical chart review. This study was approved by institutional review boards of the collaborating hospitals. The multivariate Cox proportional hazards model was performed to investigate prognostic factors for disease-free survival (DFS) and overall survival (OS). All statistical analyses were performed using the Statistical Analysis Software for Windows, version 9.1 (SAS Institute, Cary, NC, USA).

Results: UTUC patients had higher proportions of advanced clinical stage (T2–4) and poor cell differentiation (G3). Bladder cancer patients with advanced clinical stages (T2–3 and T4) had increased risks of poorer OS (hazard ratio, HR = 1.7 and 3.9, respectively). UTUC patients with the advanced clinical stage (T4) had a significantly greater risk of poorer OS (HR = 8.7). Bladder cancer patients with a high grade (G2–3) had a significantly increased risk of poorer OS (HR = 3.8).

Conclusion: Based on the limited parameters and heterogeneous data, the present study merely observed that bladder cancer and UTUC patients with the higher tumor stage have a significant increased risk of poor overall survival. Therefore, the causal mechanisms of UC prognosis remained to be further explored in a larger population.

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Keywords: Bladder cancer; Prognostic factors; Survival; Upper urinary tract; Urothelial carcinoma

Conflicts of interest: The authors declare that they have no conflicts of interest related to the subject matter or materials discussed in this article.

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1. Introduction

Urothelial carcinoma (UC) can arise from the urothelium of the urinary tract, including the bladder, renal pelvis, and ureter. Bladder cancer is the second most common malignancy of the genitourinary tract and is the eighth most common cause of male malignancy in Taiwanese population.¹ Conversely, urothelial carcinoma of the upper urinary tract (UTUC) of the renal pelvis and ureter is a rare and heterogeneous disease that accounts for approximately 5% of all UC patients.² According to the Taiwan Cancer Registry Annual Report in 2013, the age-standardized incidence rate of UTUC per 100,000 population was 4.09 in men and 4.37 in women. Therefore, UTUC is a relatively uncommon cancer type in Taiwan. Research has shown that Taiwanese men were two times more likely to have UTUC than women in other Western countries,^{3–5} while the male-to-female ratio is 1:1.2 in Taiwanese population.^{6–9} Although UTUC of the renal pelvis and ureter is uncommon and comprises 23% of all UC patients in black-foot disease (BFD)-endemic areas with arsenic exposure in southwestern Taiwan, this phenomenon still represents a higher percentage than in other countries.^{6,10}

Several risk factors such as arsenic exposure, cigarette smoking, and exposure to hazardous chemicals are associated with UC.^{1,8} The highest incidence of bladder cancer has been found in the BFD-endemic areas in Taiwan.^{11,12} Epidemiological studies have reported that chronic arsenic exposure through drinking well water is associated with bladder cancer.^{13,14} Previous studies reported that a higher incidence of UTUC is significantly associated with arsenic exposure, cigarette smoking and occupational carcinogens.^{7,8} Cigarette smoking is the major risk factor for UC, resulting in a 2–4-fold risk among ever smokers.^{1,15,16} Chemical carcinogens exposure to occupations such as painting and working with dye are known risk factors of UC.^{1,17} Recently, our study showed that arsenic exposure, cigarette smoking, and risk genotypes of vascular endothelial growth factor contributed to a higher risk of UTUC than that of bladder cancer.⁹ These findings suggest that clinical, epidemiological and molecular differences may exist between bladder cancer and UTUC.

Despite the fact that UC is derived from the urothelium from the renal pelvis to the urethra, bladder cancer and UTUC have been proposed to represent different entities, based on their differing locations and embryonic derivation from different structures.¹⁸ UTUC has been reported to be associated with a more aggressive disease course, and frequently went undiagnosed until the more-advanced stages relative to bladder cancer.^{19–22} A better understanding of the differences between bladder cancer and UTUC might help to guide clinical decision-making. Therefore, the aim of this study was to identify the clinical and demographic characteristics for bladder cancer and UTUC in a Taiwanese population.

2. Methods

2.1. Study participants

This study consisted of 736 study participants and was conducted between September 1998 and December 2009. All histopathologically confirmed UC cases including 470 patients with bladder cancer and 266 patients with UTUC, who were recruited from the Department of Urology by way of collaborative hospitals. Pathological confirmation of UC was performed by customary urological practices that include endoscopic biopsy and surgical resection of urinary tract cancers. Based on the World Health Organization (WHO) grading system, the histopathological characteristics of UC was classified into 3 tumor grades (G1–3). Tumor staging of patients (stages T1–4) was classified using the 1997 American Joint Committee on Cancer (AJCC)-tumor node metastasis (TNM) system. In the present study, many UC patients were identified as T1 stage and not every tumor specimen was available by transurethral resection of bladder tumor (TURBT) for pathological local stage examination. Therefore, the lymph node status can not verifiably be determined by pathological examination. In addition to pathological local stage, clinical stage is evaluated by physical examination, cystoscopic tumor biopsy and any diagnostic imaging such as computed tomography (CT) scan. This testing provides available information including tumor size, infiltrative depth, and lymph nodes involvement, therefore, clinical stage is considered to be a complementary index for the assessment of relevant treatments of UC in clinical practice. All study participants received a detailed description of this study and provided written informed consent before inclusion.

2.2. Exposure information of risk factors

During the recruiting process, each study participant was interviewed in-person using a standard questionnaire to collect information including demographic characteristics, disease history, history of cigarette smoking and alcohol consumption, and exposure to hazardous chemicals such as the components of hair dye, leather, fabric, and paint. According to definitions provided by the U.S. Centers for Disease Control, individuals who had smoked in excess of 100 cigarettes during their lifetime were defined as “ever smokers” and the others were designated as “never smokers”.²³ “Ever drinkers” were recognized as subjects who had consumed alcohol 3 or more days per week for a period of at least 6 months and the others were “never drinkers”. In addition, study subjects who had been exposed to 2 or more hazardous chemicals including dye for hair, leather, fabric, or paint 7 or more times per week for a period of at least 1 month were classified as “ever exposed” and those study subjects without this exposure history were regarded as “never exposed”.

Based on previous studies regarding chronic arsenic exposure in Taiwan, we further classified the residential areas into

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