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Original article

Effect of tumor location on survival in urinary bladder adenocarcinoma: A population-based analysis

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Abstract

Purpose: To investigate the prognostic significance of tumor location on survival outcomes in patients with urinary bladder adenocarcinoma (BAC).

Methods: We retrospectively analyzed cases of BAC with known tumor location from the Surveillance, Epidemiology, and End Results database from 1973 to 2012. Data regarding patient demographics, tumor characteristics, and oncological and survival outcomes were collected. Patients were subgrouped according to tumor location into urachal/dome (dome and urachus [UD]), lateral wall (anterior, posterior, and lateral bladder walls [LW]), and base (trigone, ureteral orifices, and bladder neck [BL]).

Results: A total of 1,361 cases of BAC with known tumor location were identified. More UD tumors were low grade (grade I and II; 51%) than LW (33%) and BL (43%) tumors ($P < 0.0001$). UD lesions were the most likely to have metastatic spread (23% vs. 17% for LW and 15% for BL) ($P < 0.0001$). The 5-year overall survival (OS) and disease-specific survival (DSS) rates were 37.3% and 49.0%, respectively, for all BAC. Furthermore, the 5-year OS rates were 42.3%, 35.9%, and 28.4% for UD, LW, and BL lesions, respectively ($P < 0.0001$), whereas the 5-year DSS rates were 50.2%, 51.7%, and 42.1% for UD, LW, and BL lesions, respectively ($P = 0.0097$). Multivariate Cox regression analysis controlling for tumor stage and grade demonstrated that both tumors of the LW (hazards ratio [HR] = 1.52 for OS and 1.30 for DSS) and BL (HR = 1.71 for OS and 1.57 for DSS) conferred a worse prognosis relative to those of the UD ($P < 0.05$).

Conclusions: Tumor location of BAC is an independent prognostic factor for disease outcome. Our results suggest that the urachal and dome locations are associated with relatively favorable survival and oncological outcomes, whereas basal location confers poorer outcomes.

Keywords: Bladder cancer; Adenocarcinoma; Tumor location; Prognostic indicators

1. Introduction

Bladder cancer is the second most common cancer of the genitourinary tract. Although most bladder cancers (~90%) are urothelial (transitional cell) carcinomas (UCB), bladder adenocarcinoma (BAC) represents an uncommon variant, accounting for approximately 0.5% to 2% of all bladder cancers in the United States [1,2]. Although the incidence of BAC is higher in patients with bladder exstrophy (90%) [3] and in regions where schistosomiasis is endemic (9%–10%) [4,5], owing to the rarity of the disease, the pathogenesis and natural history of BAC have not been well characterized [2]. Historically, studies of BAC have been limited to single-center retrospective analyses with small sample sizes [6–9]. More recently, 2 larger scale analyses using the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) database have helped define prognostic factors for BAC disease outcomes, including tumor stage, grade, and lymph node metastasis [10,11]. These results

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were confirmed in a large, single-center radical cystectomy series from Mansoura, Egypt, which included all bladder cancer histopathological cell types, including BAC [5,12].

Although studies on UCB have identified tumor location within the bladder as a predictor of disease outcome [13–17], there is conflicting evidence as to whether tumor location holds similar predictive value in BAC. Some studies, including a previous SEER analysis by Wright et al. [10], suggest that urachal BAC is associated with a more favorable prognosis than nonurachal [7,18]. Other reports, however, have reported no statistically significant differences [8,11,19]. In this analysis, we examine the predictive value of tumor location on survival in patients with BAC using the SEER population-based tumor registry.

2. Methods

2.1. Patient selection

The SEER 18 database, maintained by the National Cancer Institute (Bethesda, MD), was examined for BAC cases from 1973 to 2012. SEER contains patient demographic and cancer data representing approximately 28% of the US population. As no patient identifiers are included in SEER, institutional review board approval was not necessary. We searched the database using ICD-O-3 (International Statistical Classification of Disease for Oncology, third edition) primary site codes specific to the urinary bladder and histology codes specific to adenocarcinoma. Considering the conflicting evidence regarding the prognostic value of tumor location, we decided to stratify our analysis into 3 separate regions of the bladder. Urachal and dome lesions were grouped together as "urachus/dome" (UD). Likewise, lesions of the anterior, posterior, and lateral bladder walls were grouped together as "lateral wall" (LW), whereas lesions of the trigone, bladder neck, and ureteral orifice were grouped together as "base" (BL). Tumors of overlapping subsites or unknown location were excluded.

2.2. Statistical analysis

Data exported from SEER*Stat 8.2.1 software were stored in Microsoft Excel 2011 (Microsoft Corporation, Redmond, WA). Chi-Square and ANOVA analyses were generated using JMP Statistical Discovery 12 (SAS Institute, Cary, NC). Kaplan-Meier survival curves for both the 5-year disease-specific survival (DSS) and overall survival (OS) were generated using the same software. Hazards ratios (HR) for the 5-year DSS and OS were generated using the Cox Proportional Hazards regression model. $P < 0.05$ was considered statistically significant for all tests.

3. Results

3.1. Patient demographics and tumor characteristics

A total of 2,533 cases of BAC were identified, of which 1,361 lesions had a known intravesical location (620 UD, 477 LW, and 264 BL lesions) and were included in our analysis.

The mean age at diagnosis was 64 ± 15 years. Patients with UD tumors were relatively younger (59 ± 15 years) than those with LW (69 ± 14 years) and BL (67 ± 13 years) tumors ($P < 0.0001$) and had less male predominance ($P = 0.0037$). More UD tumors were mucinous adenocarcinoma (74%) when compared with LW (26%) and BL (41%) tumors ($P < 0.0001$). More than half of UD tumors were low grade (grade I or II) (51%) upon diagnosis than LW (33%) and BL (43%) tumors ($P < 0.0001$). However, a higher percentage of UD lesions were metastatic (23%) relative to LW (17%) and BL (15%) tumors ($P < 0.0001$). A higher percentage of patients with UD lesions underwent extensive surgical management (including any type of cystectomy or pelvic exenteration) (72%) than LW (45%) and BL (48%) patients ($P < 0.0001$). Demographic data and tumor characteristics are summarized in Table 1.

3.2. Survival analyses

Univariate Kaplan-Meier analysis of all locations demonstrated 5-year OS and DSS of 37.3% and 49.0%, respectively (Table 2). Based on tumor location, the 5-year OS rates were 42.3%, 35.9%, and 28.4% for UD, LW, and BL lesions, respectively ($P < 0.0001$), whereas the 5-year DSS rates were 50.2%, 51.7%, and 42.1% for UD, LW, and BL lesions, respectively ($P = 0.0097$). Kaplan-Meier analysis of all locations demonstrated the 10-year OS and DSS rates of 21.8% and 37.4%, respectively. The 10-year OS rates were 26.7%, 19.4%, and 15.2% for UD, LW, and BL lesions, respectively ($P < 0.0001$) (Fig. A) whereas the 10-year DSS rates were 38.6%, 40.4%, and 30.0% for UD, LW, and BL lesions, respectively ($P = 0.0084$) (Fig. B). Sex, tumor location, grade, and stage were predictors for survival outcome on univariate analysis (Table 2).

Multivariate Cox regression analyses demonstrated that sex, tumor grade, stage, and location were independent prognostic factors for prediction of OS and DSS ($P < 0.05$) (Table 3). Considering OS, BL (HR = 1.71; 95% CI: 1.39–2.10; $P < 0.0001$) location conferred the worst prognosis, followed by LW (HR = 1.52; 95% CI: 1.26–1.82; $P < 0.0001$) and finally UD (Table 3). As for DSS, the order was the same: BL (HR = 1.57; 95% CI: 1.23–1.98; $P = 0.0003$) location conferred the worst prognosis, followed by LW (HR = 1.30; 95% CI: 1.06–1.61; $P = 0.014$) and finally UD (Table 3).