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Original article

Clinical characteristics and outcomes of nonurothelial cell carcinoma of the bladder: Results from the National Cancer Data Base

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Abstract

Objectives: To determine the clinical characteristics, treatment patterns, and outcomes of patients with nonurothelial cell bladder cancer (NUBC) in the United States.

Methods: A total of 163,683 patients with bladder cancer from 1998 to 2014 in the National Cancer Data Base were identified. Of all, 153,262 had urothelial cell (UC) carcinoma (93.6%) and 10,421 had NUBC (6.4%) further classified as: squamous cell carcinoma (SC, 2.4%), adenocarcinoma (AC, 1.7%), neuroendocrine (NE, 1.3%), micropapillary (MP, a UC variant histology, 0.3%), lymphoid/haematopoietic (LH, 0.3%), and sarcoma/mesenchymal (SM, 0.3%). Analyses were run on the entire cohort, those with non–muscle-invasive disease (T0–1, N0, M0), muscle-invasive disease (MIBC, T2–4A, N0, M0), and metastatic disease (T4B or N+ or M+). Clinical characteristics and treatment received (surgery, chemotherapy, and radiation) were reported by histologic subtype. Survival analysis was performed via Kaplan-Meier estimates and Cox proportional hazards models.

Results: Patients with NE, SC, MP, and AC were more likely to be diagnosed with metastatic disease (11.5% for UC vs. 40%, 31.3%, 17.8%, and 30.6%, respectively, $P < 0.001$). Patients with NUBC were also more likely to have MIBC compared to UC (43% vs. 32.5%, respectively). For all patients, those with UC may be less likely to undergo cystectomy, chemotherapy, and radiation therapy ($P < 0.001$). For all patients, NUBC, with the exception of LH, SM, and MP, was associated with inferior survival compared to UC ($P<0.001$).

Conclusions: This encompassing clinical characterization and prognosis of NUBC patients in the United States shows NUBC patients have significantly different disease characteristics compared to those with UC, and present with more advanced disease, receive more treatment, and overall have inferior outcomes. Further work is needed to help improve outcomes for these patients.

Keywords: Bladder cancer; Histology; Radiation therapy; Cystectomy; Chemotherapy

1. Introduction

There are over 75,000 new cases of cancer of the urinary bladder in the United States each year, accounting for over 16,000 deaths. Bladder cancer is the fourth most common cancer in American men [1]. Greater than 90% of these cases are urothelial cell carcinomas (UC). The remainder is composed of other histologies such as squamous cell carcinoma, adenocarcinoma, neuroendocrine carcinoma, and sarcomatoid malignancies, among others [2]. The epidemiology, prognosis, and treatment options for UC of the bladder have been widely characterized while there is a dearth of data on nonurothelial cell bladder cancers (NUBC) [3]. The limited data on NUBC presents a challenge for clinicians and patients attempting to make informed treatment decisions when facing this diagnosis. Therefore, we analyzed the presentation, treatment patterns,

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and outcomes of patients with NUBC in the United States using the National Cancer Data Base (NCDB).

2. Materials and methods

2.1. Data source

The NCDB is a national hospital-based registry jointly sponsored by the American College of Surgeons and the American Cancer Society. It collects data from more than 1,500 Commission on Cancer-accredited facilities and captures approximately 70% of incident cancers in the United States annually. The data accuracy and quality is continually validated via data quality reviews, site surveys, and internal monitoring [4]. Methods regarding data coding have been described elsewhere [5]. This study was granted exempt review by the Institutional Review Boards of the Morehouse School of Medicine, Atlanta, GA.

2.2. Study population

We selected patients aged ≥18 with a diagnosis of first primary bladder cancer (*International Classification of Diseases for Oncology, Third Edition* [ICD-O-3] site code: C67.0–C67.9) between January 1, 1998 and December 31, 2014 who had at least part of their initial treatment course at a Commission on Cancer-accredited facility. Detailed patient selection schema is shown in Fig. 1.

2.3. Measurement

This study examined the characteristics, treatments, and outcomes of bladder cancer patients by histology group. Defined by the NCDB as the dominant histology present via ICD-O-3 codes, histologies were grouped into the following: urothelial cell (UC), squamous cell (SC), adenocarcinoma (AC), neuroendocrine or small cell (NE), micropapillary variant urothelial cell (MP), sarcoma or mesenchymal (SM), and lymphoid or haematopoietic (LH). Patients with unspecified histology were excluded. Bladder cancer types were grouped by clinical stage at diagnosis into non–muscle-invasive bladder cancer (NMIBC) (T1, N0, M0), muscle-invasive bladder cancer (MIBC) (T2–T4A, N0, M0), metastatic (T4B or N+ or M+), and other (SM and LH histologies, because they did not have comparable tumor-node-metastasis clinical staging data). Surgical procedure was captured by site-specific surgery codes in the NCDB and categorized as no surgery, transurethral resection of bladder tumor (TURBT), partial cystectomy, or complete cystectomy (simple, total, or radical cystectomy). Patients categorized as having a

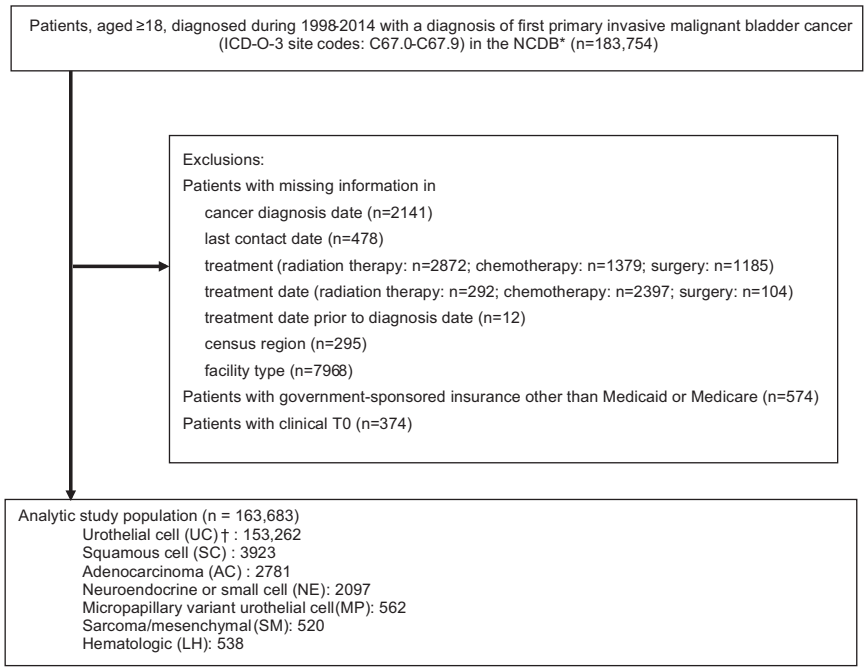

Fig. 1. Patient selection schema.