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Original article

Neoadjuvant chemotherapy administration and time to cystectomy for muscle-invasive bladder cancer: An evaluation of transitions between academic and community settings

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Abstract

Objectives: Neoadjuvant chemotherapy (NAC) before radical cystectomy is the standard of care for muscle-invasive bladder cancer (MIBC). Many patients are referred to an academic medical center (AMC) for cystectomy but receive NAC in the community setting. This study examines if administration of NAC in the community is associated with differences in type of NAC received, pathologic response rate (pT0), and time to cystectomy as compared to NAC administered at an AMC.

Methods: We performed a retrospective study of patients with MIBC (cT2a-T4-Nx-M0) referred to a single AMC between 1/2012 and 1/2014 who received NAC. We analyzed chemotherapy received, time to cystectomy, pT0, and survival in patients who received NAC in our AMC compared to those treated in the community.

Results: In all, 47 patients were analyzed. A similar total dose of cisplatin (median: 280 mg/m^2 for both groups, $P = 0.82$) and pT0 rate (25% vs. 29%, $P = 0.72$) were seen in patients treated in our AMC and the community. However, administration of NAC in the community was associated with a prolonged time to cystectomy compared with that in our AMC (median number of days 162 vs. 128, $P < 0.01$). This remained significant after adjusting for stage, comorbidity status, and distance to the AMC ($P = 0.02$). Disease-free survival and overall survival did not differ.

Conclusion: Patients with MIBC treated with NAC in the community as compared to an AMC received similar chemotherapy and achieved comparable pT0 rates, indicating effective implementation of NAC in the community. However, NAC in the community was associated with longer time to cystectomy, suggesting a delay in the transition of care between settings.

Keywords: Cystectomy; Neoadjuvant therapy; Urinary bladder neoplasms; Time factors; Quality indicators

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1. Introduction

Bladder cancer is the 6th most common cancer in the United States, with an estimated 74,690 new cases and 15,580 deaths for 2014 [1]. Although most cases are noninvasive at initial diagnosis, nearly 25% of these cases progress to muscle-invasive bladder cancer (MIBC) and 20% to 30% of patients have MIBC at the time of diagnosis [2].

Treatment of MIBC requires coordinated multidisciplinary care that often stretches across practice settings. Neoadjuvant chemotherapy (NAC) before radical cystectomy represents a standard of care for MIBC based on randomized clinical trials and a meta-analysis [3–5]. The gradual but steady increase in implementation of NAC over the last 15 years has made transitions in care more common and important [6]. Many patients are referred to an academic medical center (AMC) upon diagnosis of MIBC for consideration of cystectomy because many community urologists do not routinely perform cystectomies, and centers with high surgical volume have improved perioperative mortality and long-term mortality rates [7–9]. Many of these patients return to community oncologists for NAC before cystectomy, with others receiving NAC at the AMC in which they undergo surgery.

Treatment of patients with MIBC at different centers raises a potential issue of treatment coordination and delays [10,11]. A treatment delay of more than 3 months from initial diagnosis to cystectomy has been associated with decreased overall survival (OS) in several studies of patients who did not receive NAC [12,13]. There is also an association of a treatment delay with worse pathologic stage at the time of cystectomy [12–19]. An association of delay with adverse outcomes in patients receiving NAC, however, is less well studied.

It is not known if patients who are referred to the community setting for NAC have a delay in cystectomy compared with patients who remain at the referral AMC for NAC. It is also not known if delay to cystectomy is associated with a decrease in survival or pathologic response rate (pT0) in patients who receive NAC in these different settings. The goals of this retrospective study are to examine time to cystectomy, chemotherapy received, pT0, and survival in patients who receive NAC before cystectomy in the community setting compared to an AMC.

2. Materials and methods

2.1. Study population

We performed a retrospective chart review at a single academic institution using the University of North Carolina Genitourinary OncoLogy Database (UNC GOLD) [20], a clinical database that captures all patients seen in the UNC multidisciplinary genitourinary oncology clinic. This study was approved by the Institutional Review Board at UNC.

A query of UNC GOLD for all MIBC (T2-T4-Nx-M0) cases between January 1, 2012 and January 2, 2014 revealed 94 patients recommended to undergo cystectomy at their initial visit after diagnosis. A medical record chart review of these patients revealed that 47 of 94 patients (50%) received NAC—these patients formed our study cohort. Of those who did not receive NAC, the most common reasons included renal dysfunction (26%), patient preference (21%), and hearing loss (14%).

2.2. Study variables

Data collected included patient demographics, stage, comorbidity score, site of NAC delivery (i.e., AMC or community), chemotherapeutic regimen, time to cystectomy, pathologic response rate, disease-free survival (DFS), and OS. Time to cystectomy was calculated from the day of initial consultation with medical oncology at our institution to the day of cystectomy. Stage was determined by American Joint Committee on Cancer TNM stage recorded before NAC (clinical stage) and after cystectomy (pathologic stage). Comorbidity score was calculated using age-adjusted Charlson Comorbidity index score [21]. Distance to the AMC was calculated from the site of each patient's residence to our institution. The date of cessation of NAC was defined as the last date the patient received any chemotherapy. The NAC regimen for each patient was recommended by the medical oncologist at our AMC for all patients. Pathologic response rate was defined as pT0 (pT0-N0-M0) at the time of cystectomy. Rate of $<$pT2 (pT0-T1-N0-M0) at the time of cystectomy was also examined. Patients with available data were evaluated for bladder cancer progression/recurrence and survival.

The primary exposure variable was whether NAC was given at AMC or a community oncology practice. The primary outcome was time to cystectomy from date of initial visit at AMC. Secondary outcomes were pathologic response rate and total dose of cisplatin received with NAC, DFS, and OS.

2.3. Statistical analysis

Descriptive statistics were obtained for continuous and categorical variables. Means and standard deviation were used for continuous variables and frequencies for categorical variables. Fisher's exact tests were used to compare categorical variables and Wilcoxon rank sums were used for continuous variables. Multivariable linear regression was used for the model with outcome of time to cystectomy in days. Cox proportional hazards analysis was used for DFS and OS calculations. All statistical analysis was conducted using SAS software (SAS Institute Inc., Cary, NC) and a $P < 0.05$ was considered statistically significant.