

# The Association between Mortality and Distance to Treatment Facility in Patients with Muscle Invasive Bladder Cancer



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## Abbreviations and Acronyms

MIBC = muscle invasive bladder cancer

NAC = neoadjuvant chemotherapy

NCDB = National Cancer Database

RC = radical cystectomy

**Purpose:** Regionalization of bladder cancer treatment is suggested to improve quality of care. As an unintended consequence some patients travel farther for care with unknown implications on outcomes. We characterized the relationship between distance and overall mortality in patients with invasive bladder cancer and those who underwent radical cystectomy.

**Materials and Methods:** We performed a retrospective cohort study using NCDB (National Cancer Database) from 2004 to 2012 to identify patients with muscle invasive bladder cancer (cT2a-T4 N0 M0). We also extracted a subgroup of patients who underwent radical cystectomy. Multivariate Cox proportional hazards and multinomial logistic regression analyses were performed in each group, controlling for demographic, clinical, hospital and geographic factors.

**Results:** For 34,729 patients with muscle invasive bladder cancer traveling farther for treatment was associated with a lower probability of overall mortality (referent less than 12.5 miles, 12.5 to 49.9 miles HR 0.96, 95% CI 0.92–0.99 and 50 to 249.9 miles HR 0.91, 95% CI 0.86–0.96). This was significant for patients with cT2 disease and those treated at academic centers ( $p \leq 0.05$ ). For 11,059 patients who underwent radical cystectomy this trend did not reach significance. However, longer distance was associated with surgery at a high volume institution and receipt of neoadjuvant chemotherapy (each  $p < 0.001$ ).

**Conclusions:** Patients who traveled farther for bladder cancer treatment did not experience inferior survival outcomes and traveling to academic institutions was associated with reduced mortality. For patients who undergo cystectomy this relationship was equivocal, although longer distance was associated with receiving neoadjuvant chemotherapy or surgery at a high volume facility. These findings may reflect a complex association of regionalization of bladder cancer care with patient individual health and health care seeking behavior.

**Key Words:** urinary bladder, carcinoma, mortality, health services accessibility, neoadjuvant therapy

BLADDER cancer is the sixth most common cancer in the United States, causing an estimated 74,000 new cases and 16,000 deaths per year.<sup>1</sup> RC is the gold standard treatment of MIBC

without evidence of metastasis.<sup>2</sup> NAC is an underused treatment that increases survival in select patients.<sup>3,4</sup>

This multidisciplinary approach to MIBC management coincides with

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increasing regionalization of bladder cancer surgery to high volume centers.<sup>5,6</sup> As an unintended consequence some patients travel farther for care.<sup>7,8</sup> Geographic barriers to care have been described for other solid cancers and are associated with worse prognosis and higher mortality.<sup>9–12</sup> Fewer studies have shown that patients who travel farther for cancer care have improved outcomes.<sup>13,14</sup>

There is scant literature regarding the relationship between MIBC and the distance to care. A small, single institution study of patients treated with RC demonstrated an increased risk of mortality with distance<sup>15</sup> but other studies did not directly evaluate the distance-mortality relationship.<sup>4,7,16–19</sup>

We attempted to better define this relationship. Based on existing literature on lung, breast, gastrointestinal and bladder cancers<sup>4,7,8,10,12,16–19</sup> we hypothesized that a longer distance to the treatment facility would be associated with an increased probability of mortality in patients with MIBC. In the RC subgroup we hypothesized that travel distance would be associated with higher mortality and decreased receipt of NAC.

## MATERIALS AND METHODS

### Patient Selection

Data from 2004 through 2012 were abstracted from NCDB, a nationwide oncology registry with information on more than 70% of incident cancers in the United States. Included in study were 366,387 patients with histologically proven urothelial carcinoma of the bladder, which was identified based on ICD-0-3 morphological codes 8120, 8122 and 8130.

We identified 2 cohorts. The first cohort included 34,729 patients with locally invasive bladder cancer (cT2–cT4a, N0M0) based on the AJCC (American Joint Committee on Cancer) Cancer Staging Manual, 7th edition. Study exclusion criteria included cT4b disease, positive or unknown nodal status, metastatic disease, incomplete followup, unknown distance to a facility, primary management with palliative care, treatment outside CoC (Commission on Cancer) or at an “other” facility, distance from care 250 miles or greater and age less than 40 years (suppressed in NCDB). The supplementary figure (<http://jurology.com/>) shows selection criteria. A subgroup of 11,059 patients was identified in whom RC was done as definitive treatment.

### Variables and End Points

Our primary exposure variable was the distance traveled for treatment. The great circle distance was calculated with the Haversine formula to estimate the distance from the ZIP Code™ of the patient residence to the address of the diagnosing institution. Using prior literature, travel distance was categorized as short—less than 12.5, intermediate—12.5 to 49.9 or long—50.0 to 249.9 miles.<sup>10,20</sup>

Other variables included year of diagnosis, age at diagnosis, gender, race/ethnicity, Charlson-Deyo comorbidity

index, income (ZIP Code median income quartile), education (percent of ZIP Code inhabitants without a high school diploma), insurance status, metropolitan status, clinical T stage, geographical region and treatment facility. Facility types included community cancer programs with 100 to 500 patients annually, comprehensive community cancer programs with more than 500 patients annually, academic programs with more than 500 patients annually and with graduate medical education, and INCP (Integrated Network Cancer Program), a group of facilities providing cancer care. For the RC subgroup additional variables included receipt of NAC and hospital volume by the annual number of cases.

The primary end point was the probability of overall mortality in each cohort. The secondary outcome of the study was hospital volume and receipt of NAC in the cystectomy cohort.

### Statistical Analysis

Frequencies and proportions were generated for categorical variables and stratified by distance. The chi-square test was used to assess the statistical significance of differences in proportions. All ORs, HRs, 95% CIs and p values were calculated with SAS™, version 9.4. Statistical significance was considered at  $p < 0.05$ .

Mortality was examined by the Kaplan-Meier method and the log rank test. A multivariate Cox proportional hazards model was fit for the association of travel distance with mortality when controlling for covariates. SEs were clustered at the facility level to capture possible correlations. All subgroup analyses were planned a priori, including stratification by clinical stage and 2-way interaction analysis for distance and facility type to assess the significance of this relationship on overall mortality.

In the RC subgroup receipt of NAC was evaluated in multivariate logistic regression models. Two-way interaction analyses were performed for distance and facility type. Multinomial logistic regressions were used to test 2 models simultaneously for the association of distance with 1) clinical stage and 2) hospital volume.

An institutional review board waiver in accordance with the use of de-identified administrative data was obtained prior to performing this study.

## RESULTS

### Demographics and Distance Traveled

The final sample consisted of 34,729 patients with MIBC, of whom 11,059 underwent RC (supplementary table 1, <http://jurology.com/>). In the full cohort 58.3% of patients lived a short distance (less than 12.5 miles), 29.9% lived an intermediate distance (12.5 to 49.9 miles) and 11.8% lived a long distance (50 to 249.9 miles) from the treatment facility. In the RC subgroup 42% lived a short distance, 35.3% lived an intermediate distance and 22.7% lived a long distance from the treatment facility. The median distance traveled by all patients was 9.6 miles (IQR 4.1–25.3), which increased during the study period. In each sample patients tended to be male, older,

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