



## Contemporary 90-day mortality rates after radical cystectomy in the elderly

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### Abstract

**Introduction:** Existing radical cystectomy (RC) perioperative mortality estimates may underestimate the contemporary rates due to more advanced age, more baseline comorbidities and potentially broader inclusion criteria for RC, relative to past criteria.

**Methods:** Within the most recent Surveillance, Epidemiology, and End Results (SEER)-Medicare database we identified clinically non-metastatic, muscle-invasive (T2–T4a) urothelial carcinoma of the urinary bladder (UCUB) patients, who underwent RC between 1991 and 2009. Mortality at 30- and 90-day after RC was quantified. Multivariable logistic regression analyses tested predictors of 90-day mortality.

**Results:** Within 5207 assessable RC patients 30- and 90-day mortality rates were 5.2 and 10.6%, respectively. According to age 65–69, 70–79 and  $\geq 80$  years, 90-day mortality rates were 6.4, 10.1 and 14.8% ( $p < 0.001$ ). Additionally, 90-day mortality rates increased with increasing Charlson Comorbidity Index (CCI, 0, 1, 2 and  $\geq 3$ ): 6.3, 10.3, 12.6 and 15.9% ( $p < 0.001$ ). 90-day mortality rate in unmarried patients was 13.0 vs. 9.3% in married individuals ( $p < 0.001$ ). In multivariable logistic regression analyses, advanced age, higher CCI, low socioeconomic status, unmarried status and non organ-confined stage were independent predictors of 90-day mortality (all  $p < 0.05$ ).

**Conclusions:** The contemporary SEER-Medicare derived 90-day mortality rates are substantially higher than previously reported estimates from centers of excellence, and even exceed previous SEER reports. More advanced age, higher CCI score, and other patient characteristics that distinguish the current population from others account for these differences.

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### Introduction

Radical cystectomy (RC) represents a highly morbid procedure and predisposes to non-negligible postoperative mortality (PM). A wide range of PM rates can be

ascertained from existing literature. For example, European and Japanese centers of excellence report PM rates as low as 0.6–0.8% at 30-days after RC.<sup>1,2,3,5</sup> The same authors report a doubling of PM rate, when 90-day mortality is reported: 2.0 vs. 0.8% instead of 30-day mortality.<sup>2</sup> These rates are similar to reports from the Nationwide Inpatient Sample (NIS) where RC PM ranges from 0.8% for neobladder patients to 3.0% for patients with any diversion-type treated at non-academic institutions.<sup>3,4</sup> The NIS PM rates

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apply to hospital admissions only and fail to consider events that may occur after hospital discharge.

To circumvent the limitation related to the use of an excessively short-term mortality endpoint, mortality at 90-days after surgery was reported from the Memorial Sloan-Kettering Cancer Center and showed a 3.0% rate.<sup>5</sup> Population-based reports that focused on PM at 90-days demonstrated rates from 5.4 to 8.4% according to hospital volume (low, intermediate vs. high), within the Washington State data.<sup>6</sup> Similarly, 90-day mortality rates ranged from 5.7 to 8.0% according to hospital volume within the National Cancer Database.<sup>7</sup> Taken together, these data illustrate the importance of the time point used for the calculation of PM. The latter affects the recorded rate. Moreover, even when the same time point is used important variability may persist, depending on patient characteristics, such as age, comorbidities, tumor stage, race, insurance status or income.<sup>7–9</sup> Based on these limitations, we performed an in-depth analysis of RC PM rates using the most contemporary Surveillance, Epidemiology, and End Results (SEER)-Medicare dataset. Specifically, we assessed 30- and 90-day mortality rates. Additionally, we focused on differences that may distinguish between 90-day mortality rates in older, sicker or lower socioeconomic status (SES) patients vs. others. Our hypothesis stated that an increasingly larger proportion of older and sicker patients were treated with RC over time and that 90-day mortality rates will substantially exceed those recorded at 30-days. Moreover, we postulated that 90-day mortality rates would increase with age, comorbid conditions, lower SES and more advanced tumor stage.

## Patients and methods

### Study source

The current study relied on the SEER-Medicare linked database. This database is 98% complete for case ascertainment. The SEER registries identify 28% of all incident cancer cases in the United States. Medicare insures approximately 97% of all Americans aged  $\geq 65$  years. Linkage to the SEER database is complete for approximately 93% of cases.<sup>10</sup>

### Study population

Overall 15,080 patients with clinically non-metastatic (cNOM0) muscle-invasive (stage T2–T4) urothelial carcinoma of the urinary bladder (UCUB) (International Classification of disease for Oncology [ICD–O] site code 67.0, histologic code 8120 or 8130), with or without lymph node metastases at final pathology, diagnosed between January 1991 and December 2009, with follow-up until December 31, 2011 were abstracted. Patients not enrolled in Medicare parts A or B for a minimum of 12 months prior to their first recorded diagnosis and for 6 months after

diagnosis were not considered. Patients who had health maintenance organization enrollment in the year prior to diagnosis or for any period following diagnosis were also excluded. To ensure that all subjects had at least 1 year of claims from which comorbidities are derived, only those aged  $\geq 66$  years old were considered. Additional exclusions comprised of those with unknown race ( $n = 36$ ), and unknown marital status ( $n = 432$ ). Furthermore, patients treated with surgery  $\geq 6$  months after diagnosis were also not considered in the current study ( $n = 1185$ ). Finally, patients with stages T4b or T4 not otherwise specified were omitted from our analyses, as the current guidelines suggest a different management approach for such individuals ( $n = 477$ ). This resulted in 5207 assessable individuals with T2–T4a, pN0, Nx and pN+ patients.

### Covariates

Covariates comprised age at diagnosis, comorbidities (derived using a validated algorithm based on the Charlson comorbidity index [CCI]<sup>11</sup>), organ-confined (OC) UCUB (T2N0/X) and non organ-confined (NOC) UCUB (T3–T4a and/or N+), tumor grade (low-, high-grade), gender, race (white, black, other), marital status (married, unmarried), socioeconomic status (SES) (composite variable of income, education, and poverty levels<sup>12</sup>), year of diagnosis, urban residence status (non-, metropolitan) and administration of neoadjuvant chemotherapy (NC). Patients that had chemotherapy claims within 6 month of diagnosis and a claim for cystectomy within 180 days of the first chemotherapy claim were categorized as recipients of neoadjuvant chemotherapy.

### Statistical analyses

Means, medians and interquartile ranges were reported for continuous variables. Frequencies and proportions were reported for categorical variables. The Mann–Whitney and chi-square tests were used to compare the statistical significance of differences medians and proportions, respectively. Subsequently, univariable and multivariable logistic regression analyses were performed to identify the clinical and demographic characteristics associated with 90-day mortality. All statistical tests were performed using R software environment for statistical computing and graphics (Vienna, Austria, version 3.0.1). All tests were 2-sided with a significance level set at  $p < 0.05$ .

## Results

### Baseline characteristics

Overall, 5207 patients with non-metastatic muscle-invasive UCUB who underwent RC were included in the study cohort (Table 1). Mean (median) age at diagnosis was 75.5 (75.0) and ranged from 66 to 95 years (interquartile range:

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