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Conditional survival of patients with urothelial carcinoma of the urinary bladder treated with radical cystectomy

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ABSTRACT

Aim of study: To examine the impact of survival probability according to duration of survivorship following radical cystectomy (RC) in patients diagnosed with urothelial carcinoma of the urinary bladder (UCUB).

Methods: Overall, 4991 UCUB patients who underwent RC were abstracted. The cumulative survival estimates were used to generate conditional survival rates. Cox regression analyses were performed for prediction of cancer-specific mortality (CSM), according to duration of survivorship.

Results: The five-year CSM-free survival rate was 63.9% at RC, and increased to 71.0%, 77.5%, 81.7%, 85.9% and 86.3% in patients who survived ⩾1, 2, 3, 4 and 5 years, respectively. Patients with pT2–4 disease benefitted from the highest increase in survivorship two years after RC. The same findings were recorded according to patients' nodal status.

Conclusion: The survival of the first two years after RC markedly improves individual patient prognosis. The prognostic gains differ according to patient and tumour characteristics.

1. Introduction

Urothelial carcinoma of the urinary bladder (UCUB) is the fourth commonest cancer in the United States.[1] Radical cystectomy (RC) is the preferred standard of care for patients with muscle-invasive or refractory non-muscle-invasive disease.[2,3] Nonetheless, UCUB has an unfavourable prognosis, with 5-year recurrence-free and cancer-specific mortality (CSM)-free survival rates that range between 60–68% and 65–67% in patients with muscle-invasive UCUB (⩾pT2), respectively.[4–7] However, these survival estimates might not be informative for long-term follow-up given that the risk of death due to the disease is often highest during the initial years of follow-up after RC. This effect, otherwise known as

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conditional survival (CS), has been previously examined and reported in other malignancies.[8–12] CS rates provide an accurate evaluation of the patient's changing risk over time. Moreover, they are helpful for clinicians in the planning of appropriate follow-up after initial diagnosis and treatment.

To date, no study has examined the effect of CS in patients with UCUB. To address this void, we set to evaluate the CS rates of UCUB patients treated with a RC, using a contemporary population-based cohort originating from the United States.

2. Materials and methods

2.1. Data source

The current study relied on the Surveillance, Epidemiology and End-Results (SEER) Medicare insurance program linked database. The SEER regions represented approximately 14% of the United States population prior to the year 2000 and 26% thereafter.[13] The Medicare-linked database is 98% complete for case ascertainment. It encompasses approximately 97% of persons aged 65 years or older in the United Sates. Linkage to the SEER database is complete for roughly 93% of the patients. The SEER relies on 17 population-based cancer registries that collect data on incident of cancer cases, with information on date of diagnosis, site and extent of the disease, as well as patient and sociodemographic characteristics, vital status and follow-up.

2.2. Study population

Patients with a primary diagnosis of non-metastatic UCUB (C67.0–67.9) between years 1992 and 2005 who underwent a RC were abstracted. To ensure that all individuals had $\geqslant$1 full year of claims prior to diagnosis, only those aged $\geqslant$66 years were included. Only patients with both Medicare Part A and Part B claims available 12 months before the first recorded diagnosis and 6 months after diagnosis, and who were not enrolled in a health maintenance organization (HMO) throughout the duration of the study period were included. UCUB diagnoses based on autopsy and/or death certificate, or if their original or current reason for Medicare entitlement was listed as disability or Medicare status code including disability, were removed from the study. This resulted in an overall study population of 4991 patients.

2.3. Treatment type

Treatment type was identified by searching Part A and Part B Medicare files, and the outpatient claims file, using the ICD–9 or CPT–4 codes. Patients who underwent RC were identified via the following ICD–9 procedure codes: 57.5, 57.6, 57.71 and 57.79 or CPT–4 codes: 51550–51597. Subjects who underwent surgery in combination with radiotherapy (RT) were also identified (ICD–9: 92.0, V580, V661 and V771, CPT–4: 77261, 77399, 77400, 77490, 77750 and 77797). Patients who had chemotherapy were identified using ICD–9 diagnostic codes (V58.1, V60.2 and V67.2), procedure code (99.25) or CPT–4 codes (96400–96549). Patients who received neoadjuvant chemotherapy were selected given that a chemotherapy code occurred within 6 months of UCUB diagnosis and a RC code within 180 days following the first chemotherapy claim. Patients who received adjuvant chemotherapy were selected given that an RC code occurred within 6 months of UCUB diagnosis and a concurrent chemotherapy code within 90 days of RC.

2.4. Patient characteristics

Patient age at diagnosis was obtained from the Medicare file. Information on sex and race was obtained using the SEER demographic datafile. Subject comorbidity was quantified using the Klabunde modification[14] of the Charlson comorbidity index (CCI).[15] Tumour stage and grade, as well as nodal stage were also obtained.

2.5. Outcomes

The underlying cause of death information was obtained from SEER records.[16] UCUB deaths (ICD–9: 188.0) were classified as cancer-specific mortality (CSM). Data on CSM were available through the end of 2007. Survival was defined as the interval from the date of diagnosis to the Medicare date of mortality.

2.6. Statistical analyses

First, we estimated survival probabilities using the Kaplan–Meier method. Second, we calculated the CS estimates using the multiplicative law of probability stratified according to each available covariate.[9] For example, given that a patient has survived 2 years, what is the probability of surviving an additional 5 years. As such, the conditional 5-year CSM-free survival rate is calculated by using the 7-year cumulative survival rate divided by the 2-year cumulative survival rate.

Third, Cox regression models were fitted for prediction of CSM. To examine the plausible variation for risk of CSM, separate Cox regression models were fitted in patients who survived $\geqslant$1, 2, 3, 4 and 5 years after RC. Adjustment was made for age (<75 versus $\geqslant$75), sex (male versus female), race (white versus black versus other), baseline comorbidity (0 versus 1 versus $\geqslant$2), pathological tumour stage (pT1/a/is versus pT2 versus pT3 versus pT4), nodal status (pN0 versus pN1 versus pN2–3 versus pNx), tumour grade (low versus high versus unknown), neoadjuvant chemotherapy, adjuvant chemotherapy, radiotherapy and year of surgery. All tests were two-sided with a statistical significance set at $P < 0.05$.

3. Results

3.1. CS in the entire population

Overall 4991 UCUB patients who underwent RC were identified (Table 1). The mean follow-up was 117 months (median: 167). The total number of deaths due to UCUB was 1717. Of those, 1098 (63.9%) died within two years after RC. After RC, the baseline overall five-year CSM-free survival rate was 63.9% (95% confidence intervall (CI) = 62.4–65.4, Fig. 1). Given a 1-, 2-, 3-, 4- and 5-year survivorship, the five-year CSM-free survival probabilities were improved by +7.1 (71%),+6.5 (78%),+4.2 (82%),+4.2 (86%) and +0.4% (86%), respectively.