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Differential effect on survival of pelvic lymph node dissection at radical cystectomy for muscle invasive bladder cancer

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Abstract

Purpose: To compare long-term cancer outcomes after radical cystectomy (RC) alone or RC with pelvic lymph node dissection (PLND) according to different age and comorbidities categories.
Methods: Using the SEER-Medicare dataset, 3314 patients diagnosed with urothelial carcinoma of the urinary bladder and treated with RC alone or RC with PLND were identified. After propensity score matching to reduce potential selection bias, all cause mortality (ACM)-free and cancer specific mortality (CSM)-free survival rates were estimated. Multivariable regression models (MVA) addressed the effect of PLND on ACM and CSM. Subgroups analyses according to age and comorbidities were performed.
Results: After matching, 688 and 688 patients treated with RC alone or RC with PLND remained. The 5-year ACM-free survival rate was 36 after RC alone and 45% after RC with PLND ($p < 0001$). In MVA, PLND exerted a protective effect on ACM (HR 0.77, $p < 0.001$). The 5-year CSM-free survival rate was 54 after RC alone and 65% after RC with PLND ($p < 0.001$). In MVA, PLND exerted a protective effect on CSM (HR 0.71, $p < 0.001$). Similar results were observed in younger (age $\leq$75) and healthier (CCI = 0) patients, where PLND exerted a protective effect on ACM (HR 0.64, $p = 0.001$) and CSM (HR 0.65, $p = 0.01$). Conversely, in older (age >75) and sicker (CCI $\geq$1) patients, PLND was not associated with ACM (HR 0.98, $p = 0.8$) or CSM (HR 1.01, $p = 0.9$).
Conclusions: RC with PLND is associated with improved all cause and cancer specific survival in younger and healthier RC candidates but not in older and sicker patients.

Keywords: Radical cystectomy; Pelvic lymph node dissection; Bladder cancer; Long-term survival

Introduction

According to currently available guidelines, pelvic lymph node dissection (PLND) should be invariably performed at radical cystectomy[1,2] (RC) and represents the criteria for comprehensive RC.[3] However, there is a paucity of data comparing patients treated with radical cystectomy

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plus PLND vs. radical cystectomy alone,[4,5] and more specifically, data evaluating the potential therapeutic role of PLND according to patients age and comorbidity status are still lacking.

To address this void, we examined the most contemporary version of the SEER-Medicare database with the intent of comparing long-term cancer outcomes associated with either RC with PLND or RC alone and quantifying the magnitude of the potential benefit of PLND. Our hypothesis stated RC with PLND might have a beneficial effect on urothelial carcinoma of urinary bladder (UCUB) long-term outcomes. Moreover, we hypothesized that such benefit might be consistent among different age and comorbidities status categories.

Materials and methods

Study source

The current study relied on the 1991–2009 SEER-Medicare linked database with follow-up updated until December 31, 2011. The SEER registries identify 28% of all cancer cases in the United States. Medicare insures approximately 97% of all Americans aged ≥65 years. Linkage to the SEER database is complete for approximately 93% of cases.[6]

Study population

Overall 15,080 patients with a primary non-metastatic muscle-invasive (stage T2–T4) UCUB (International Classification of disease for Oncology [ICD–O] site code 67.0, histologic code 8120 or 8130), diagnosed between January 1991 and December 2009 were abstracted. Patient follow-up was available until December 31, 2011.

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 ≥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 ≥6 months after diagnosis were not considered in the current study, as treatment delay may confound the final results ($n = 1185$).[2] Moreover, patients with T4b or T4 not otherwise specified were omitted from our analyses ($n = 477$).[1] Final exclusions consisted of patients receiving neo-adjuvant chemotherapy or radiotherapy ($n = 442$), patients who underwent partial cystectomy ($n = 566$), patients who did not undergo a TURBT ($n = 243$) and patients without available information about PLND ($n = 603$). For the purpose of the study we focused on patients who underwent RC. This resulted in 3314 assessable individuals with T2-T4a, N0, N+ and Nx UCUB.

Study design

The study design was a retrospective case–control study, cases were patients treated with RC and PLND and controls were patients treated with RC alone.

Covariates

Demographic covariates were age at diagnosis, comorbidities derived from the Klabundle's Charlson comorbidity index (CCI) modification,[7] gender, race (white, black, other), marital status (married, unmarried), socioeconomic status (SES; composite variable of income, education, and poverty levels[8]) and population density status (urban, rural).

Cancer-related covariates comprised tumor grade and cancer stage. The latter was coded according to the AJCC staging system as tumor stage (T2, T3, T4). Lymphadenectomy-related covariates comprised nodal stage (N0, N+, Nx), number of nodes removed and number of positive nodes.

Finally, treatment-related covariate was the administration of adjuvant chemotherapy. Specifically patients who had chemotherapy claims ≤6 months prior to cystectomy and a claim for RC ≤6 months before the first chemotherapy claim were considered to have been treated either with neo-adjuvant chemo- or radiotherapy, while other patients were considered to have been treated with adjuvant chemo- or radiotherapy.

Outcomes

The primary endpoint of the study was to compare all cause mortality (ACM) and cancer specific mortality (CSM) between patients treated with RC alone and patients treated with RC with PLND.

The secondary endpoint of the study was to compare all cause mortality (ACM) and cancer specific mortality (CSM) between patients treated with RC alone and patients treated with RC with PLND according to age and comorbidity.

Statistical analyses

Means, medians and ranges were reported for continuous variables. Frequencies and proportions were reported for categorical variables. Statistical analyses consisted of three steps.

First, due to inherent differences among patients included in the two treatment groups (RC alone vs. RC with PLND), adjustment was performed using a 1-to-1 propensity score–matching ratio.[9] Propensity scores were