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Original article

Impact of positive surgical margins on overall survival after partial nephrectomy—A matched comparison based on the National Cancer Database

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Abstract

Introduction: The impact of positive surgical margins (PSM) in partial nephrectomy (PN) has been a controversy. Previous studies on the relationship between PSM and overall survival (OS) were either underpowered or had highly dissimilar groups. We used the National Cancer Database with propensity score matching to determine the association between PSM and OS after PN.

Materials and methods: We identified patients with T1/T2 N0M0 renal cancer treated with PN between 2004 and 2009, and divided them into 2 groups based on their margin status. We used propensity score matching to ensure similarities in age, comorbidity score (CCI), tumor size, histology, and grade between groups. Covariates were compared by χ^2 test. Cox multiple regression was used to estimate the hazard ratios (HR) for all-cause mortality. OS between matched groups were compared by log-rank, Breslow and Tarone-Ware tests.

Results: After excluding those with missing data on margin or survival status, 20,762 patients were eligible for matching. Each matched group had 1,265 patients, similar in age, sex, race, CCI, tumor size, histology, and grade. There were 386 recorded all-cause mortalities over a median follow-up duration of 72.6 months. Cox multiple regression showed a higher risk of all-cause mortality among cases with PSM (HR: 1.393, $P = 0.001$). Old age, high CCI, and large tumors had higher risks, while papillary and chromophore histologic subtypes had lower risks. PSM was associated with significantly worse OS by log-rank, Breslow, and Tarone-Ware tests.

Conclusion: PSM is associated with significantly worse OS after PN.

Keywords: Positive surgical margins; Overall survival; Partial nephrectomy; Matched comparison; National Cancer Database

1. Introduction

The impact of positive surgical margins (PSM) in partial nephrectomy (PN) has been a controversy. Various studies showed conflicting results regarding the associations between PSM and progression-free [1–7], cancer-specific [5,8,9], as well as overall survivals (OSs) [5,8,10]. A multicentered study [5] and a study based on the Ontario Cancer Registry [8] found no associations between PSM and OS, but the statistical powers of both studies were limited by small sample sizes. A more recent study based on the National Cancer Database (NCDB) involved a cohort of 6,038 patients who underwent PN for clinical T1 or T2 disease, and found PSM to be associated with an increased risk of all-cause mortality [10]. However, the PSM group in this study had significantly older patients with higher comorbidity scores (CCIs) compared to the negative surgical margins (NSM) group, so there might be confounding effects from other covariates. To determine the association between PSM and OS, a study that has a large sample size yet similar groups for comparison would be ideal.

Therefore, we used the latest NCDB participant user file (PUF) to determine if PSM has an impact on OS after PN in the contemporary clinical setting, with statistical matching to ensure similarities in key covariates between groups.

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2. Materials and methods

The institutional review board approved this study (protocol no.: 1611211043, approval date: December 7, 2016).

We used the NCDB PUF spanning from 2004 to 2014. To ensure that all cases for analysis had a minimum of 5 years of follow-up after PN, we only included cases between 2004 and 2009. Patients with renal cell carcinoma (RCC) were identified as those who carried the code C649 for the data item 'Primary Site', based on the International Classification of Diseases for Oncology, 3rd edition [11]. Among these cases, we selected those with clinical T1 or T2 N0M0 disease according to data items 'AJCC Clinical T', 'AJCC Clinical N' and 'AJCC Clinical M', based on the American Joint Committee on Cancer Stage Manual, 7th edition [12]. The cases were screened to identify those treated with PN, according to the data item 'Surgical Procedure of the Primary Site at any CoC Facility' with the code 30 representing PN, and were classified into 2 groups based on surgical margin status. Duration of follow-up was defined by the data item 'Last Contact or Death, Months from Dx' as the time between the date of initial diagnosis and the date on which the patient was last contacted or died, and survival status at the end of follow-up was defined by the data item 'PUF Vital Status'. Patients with missing data on surgical margin status or survival status were excluded.

The endpoint of our study was OS in the PSM and NSM groups. Covariates included age, sex, race, Charlson-Deyo CCI, tumor size, histology, and grade. Fig. 1 summarizes the process of patient selection before statistical matching.

We recoded ratio covariates into clinically meaningful categories for statistical analysis. We first performed multivariate logistic regression to identify predictors for PSM. This was followed by propensity score matching with fuzz factor set at 0, giving priority to exact matches and without replacement in sampling, to produce a PSM and a NSM group with matches for age, CCI, tumor size, histology, and grade. Covariates were compared between groups by χ^2 test, with relevant Cramer's V values to reflect effect sizes. Cox multiple regression was then used to estimate the hazard ratios (HR) of the covariates for all-cause mortality. Log-rank, Breslow, and Tarone-Ware tests were used to compare OS between matched groups. Further analyses were done among patients of specific age or with specific CCI, tumor size, histology, and grade to determine the effects of PSM in these subgroups. All statistical analyses were done using SPSS version 24.0 (IBM Corp., Armonk, NY). A $P < 0.05$ defined statistical significance throughout the study.

3. Results

A total of 21,243 patients with T1 or T2 N0M0 RCC between 2004 and 2009 underwent PN. Among them, 475 patients had unknown surgical margin status and were excluded. Of the remaining 20,768 patients, 1,279 had PSM and 19,489 had NSM. One patient from the PSM group and 5 patients from the NSM group were excluded due to missing data on survival status. Therefore, 1,278 PSM and 19,484 NSM patients were eligible for statistical matching. Propensity score matching produced 2 groups highly similar in age, sex, race, CCI, tumor size, histology and grade, with 1,265 patients in each group. Table 1 illustrates the descriptive statistics before and after statistical matching.

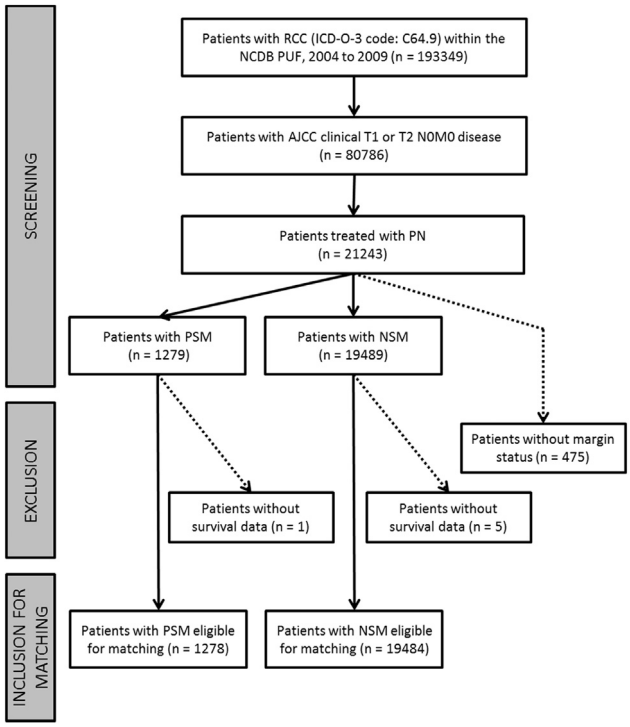

Fig. 1. Diagram showing the process of patient selection for propensity score matching. (RCC = renal cell carcinoma; ICD-O-3: International Classification of Diseases for Oncology, 3rd ed.; NCDB = National Cancer Database; PUF: participant user file; AJCC: American Joint Committee on Cancer; PN = partial nephrectomy; PSM = positive surgical margins; NSM = negative surgical margins).

Compared to the reference category of age below 50 years, most other categories of age had statistically significant odds ratios (OR) above 1 for PSM. Increasing age appeared to be associated with higher odds for PSM, with OR up to 1.800 among those aged 80 years and above. Papillary and chromophobe tumors, as well as Fuhrman grade 3 or 4 tumors, also had statistically significant OR above 1 for PSM compared to their respective reference categories. Table 2 illustrates the multivariate logistic regression model estimating the ORs for PSM among the various categories of covariates in our study.

After matching, the mean follow-up duration was 70.3 months (median: 72.6 months), with 386 recorded all-cause mortality. Cox multiple regression showed that PSM was associated with a higher risk of all-cause mortality compared to NSM (HR: 1.393, $P = 0.001$). There was a clear trend showing increasing risks of all-cause mortality