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Original article

Incidence of T3a up-staging and survival after partial nephrectomy: Size-stratified rates and implications for prognosis

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Abstract

Background: The use of partial nephrectomy (PN) to treat renal cell carcinoma has grown to include larger, more complex tumors. Such tumors are more likely to be up-staged to pT3a and generate controversy regarding the oncologic safety of PN. We aimed to estimate the proportion of patients up-staged to T3a disease after PN, stratified by clinical stage, and characterize their survival.

Methods: From 1998 to 2013, pT1-pT3aN0M0 kidney cancer patients undergoing PN or radical nephrectomy (RN) were identified from the Surveillance Epidemiology and End Results registries. Cox proportional hazards models compared cancer-specific (CSS) and overall survival (OS) for PN patients with pT1a, pT1b, and pT2 disease to stratified, up-staged pT3a patients undergoing PN. Also, we compared PN patients with up-staged pT3a disease to RN patients with pT3a disease.

Results: From the 28,854 patients undergoing PN, the estimated proportion up-staged to pT3a was 4.2%, 9.5%, and 19.5% for cT1a, cT1b, and cT2, respectively. OS was worse for tumors up-staged from cT1a to pT3a, but not for cT1b or cT2 tumors. Up-staged pT3a tumors across all stage strata demonstrated worse CSS, with worse survival for larger tumors. Analysis revealed no difference in OS or CSS for up-staged pT3a PN patients compared to pT3a RN patients.

Conclusions: A greater proportion of patients experience T3a up-staging after PN with increasing initial T stage. Up-staged pT3a patients have worse CSS across all clinical tumor stages after PN. However, our results do not demonstrate that patients up-staged after PN have compromised oncologic outcomes compared to all-comers with pT3a disease receiving RN.

Keywords: Renal cell carcinoma; Up-staging; Partial nephrectomy; Survival

1. Introduction

Over the past 2 decades, partial nephrectomy (PN) utilization has increased for the treatment of renal masses suspicious for renal cell carcinoma (RCC), particularly at high-volume centers [1,2]. The rate of PN increased most rapidly following the American Urological Association's guideline recommendation of PN for T1 disease and the swift adoption of robotic renal surgery [3,4]. Current evidence demonstrates at least equivalent survival outcomes for PN compared to radical nephrectomy (RN) for pathologically staged T1a and T1b tumors as well as well-selected T2 tumors [1,5–12]. Notably, PN is not considered appropriate management for patients with clinically apparent, locally advanced (cT3a) disease.

However, a proportion of patients with clinically localized tumors undergoing PN will be up-staged on final pathology. The growing volume of PNs has likely increased the total number of neoplasms with low clinical stage (cT1a, cT1b, or cT2 without evidence of nodal or distant metastases) that may have adverse features, including venous or perinephric tissue invasion on pathological examination [13]. However, little is known about how these up-staged tumors (e.g., cT1a to pT3a) compare to those tumors with concordant pathology (e.g., cT1a with confirmed pT1a).

The present study aims to estimate the population-based rate of up-staging of clinical disease (cT1a–cT2) to pT3a

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after PN, stratified by clinical stage (tumor size). Additionally, we hope to better understand comparative survival implications for PN patients found to have pT3a disease. We hypothesize that a greater proportion of patients will have pT3a disease after PN with increasing initial T stage (tumor size), and that those up-staged pT3a patients who received PN may represent a relatively low-risk pT3a subgroup. Hence, we expect up-staged pT3a patients receiving PN to experience worse survival compared to patients with concordant surgical pathology after PN (pT1-pT2), but potentially better survival relative to pT3a patients undergoing RN. To study this with a large sample size, we used the Surveillance Epidemiology and End Results (SEER) registry. It should be noted that SEER does not provide clinical staging, only pathologic staging. However, given that the staging of clinically localized kidney cancer is based strictly on size, our methodology is reasonable to investigate this hypothesis.

2. Methods

2.1. Study population

Patients diagnosed with stage T1a–T3a kidney cancer from 1998 to 2013 undergoing either PN or RN were included from the SEER database, which is populated by the National Cancer Institute and covers 28% of the US population. Data regarding age, demographics, year of diagnosis, tumor stage, Fuhrman grade, tumor size, surgical treatment, and survival in months (for overall survival [OS] and cancer-specific survival [CSS]) were analyzed. Patients with lymph node involvement (N+) or metastatic disease (M+) were excluded from the analyses. Additionally, we limited the maximum tumor size for the study population by excluding the largest 1% of tumors by size (i.e., tumors greater than 16 cm).

2.2. Statistical analysis

Patients undergoing PN were stratified by T1a, T1b, and T2 tumor size cutoffs (≤4, >4–7, and >7–16 cm), and the proportion of patients up-staged after PN was estimated according to identification of pathologic T3a disease. Kaplan-Meier curves estimated survival probabilities at 1-, 2-, and 5-years and comparisons used log-rank testing. Stratified by clinical T stage, OS and CSS of up-staged patients were compared to patients with concordant pathology. Additionally, within the up-staged cohort, we compared pT3a tumors of higher clinical stage (i.e., cT1b/pT3a and cT2/pT3a) to cT1a/pT3a tumors. Although PN is not the standard of care for T3a disease, we evaluated the oncologic outcomes of up-staged pT3a tumors after PN by comparing up-staged patients to all-comers with pT3a tumors after RN for OS and CSS.

Univariable and multivariable Cox proportional hazards models compared OS and CSS of the pT3a up-staged tumors to those with concordant pathology, stratified by clinical stage. Models for subanalyses explored the effect of histology and Fuhrman grade among patients with missing data or histology recorded as "other." All analyses were conducted using STATA software (v.14.0, College Station, TX).

3. Results

3.1. Cohort demographics and up-staging rates

A total of 39,104 patients met inclusion criteria with 27,275 (69.7%) undergoing PN with concordant pathology, 1,579 (4.0%) identified as up-staged to pT3a after PN, and 10,250 (26.2%) who received RN for pT3a disease. Median follow-up was 40 months (interquartile range: 18, 75). Table 1 contains demographic data, tumor size, Fuhrman grade, and histology.

Based on the proportion receiving PN for pT3a disease, the percentage of patients up-staged after PN were 4.2% for T1a, 9.5% for T1b, and 19.5% for T2 (Fig. 1). From 2000 to 2013, up-staging rates for each clinical stage stratum remained relatively constant in each year (Supplemental Table 2 and Supplemental Figure 2).

3.2. Comparative survival for localized and pT3a patients undergoing PN

Generally, patients with localized disease had higher survival probabilities compared to pT3a patients within each stratum. Unadjusted models indicated worse OS and CSS for up-staged pT3a patients undergoing PN compared to those with localized disease across all clinical stage strata. Multivariable models, adjusted for race, sex, age, tumor grade, and histology, revealed a lesser effect on OS, but maintained statistically significant worse CSS across all strata for pT3a patients (Table 2). Notably, among cT1a patients (masses ≤4 cm), pT3a up-staged patients had statistically significant worse OS (HR = 1.25 [95% CI: 1.01–1.55], $P = 0.04$) and worse CSS (HR = 1.89 [95% CI: 1.14–3.12], $P = 0.01$).

3.3. Comparative survival for up-staged pT3a patients by clinical stage

Fig. 2 illustrates lower OS and CSS rates with increasing clinical stage within the up-staged pT3a cohort, using Kaplan-Meier survival estimates. Among up-staged tumors after PN, univariable models demonstrated worse OS and CSS of cT1b/pT3a and cT2/pT3a tumors, with reference to patients' cT1a/pT3a lesions. Adjusted models showed worse OS among cT2/pT3a tumors (HR = 2.25 [95% CI: 1.43–3.53], $P < 0.01$) and worse CSS for cT1b/pT3a