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Original article

Trends in usage of cytoreductive partial nephrectomy and effect on overall survival in patients with metastatic renal cell carcinoma

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Abstract

Purpose: Cytoreductive radical nephrectomy (cRN) improves survival in select patients with metastatic renal cell carcinoma (mRCC). It is unclear, however, whether cytoreductive partial nephrectomy (cPN) compromises oncologic efficacy. We evaluated trends in utilization of cPN and compared overall survival (OS) in patients who underwent cRN or cPN for mRCC.

Materials and methods: We queried the National Cancer Database from 2006 to 2013 and identified patients who underwent cPN and cRN for mRCC. We analyzed rates of cPN over time. Logistic regression identified predictors of cPN. We matched patients based on propensity score for treatment. We used matched Kaplan-Meier survival analyses to compare OS, stratified by tumor size. We used multivariable Cox proportional hazards models to determine the effect of cPN and cRN on OS.

Results: A total of 10,144 patients met inclusion criteria, with 9,764 (96.2%) undergoing cRN and 381 (3.8%) undergoing cPN. Rates of cPN increased over time from 1.8% to 4.3% over the study period. Treatment at an academic/research facility, papillary and chromophobe histology, and more recent year of treatment were associated with increased odds of cPN. In a matched survival analysis, cPN was associated with improved OS compared with cRN (log rank, $P = 0.001$). This effect was limited to primary tumors <4 cm. In a propensity-score adjusted multivariable Cox model, cPN was associated with improved OS (hazard ratio $= 0.81$; 95% CI: 0.71–0.93; $P = 0.002$).

Conclusions: The use of cPN in patients with mRCC is increasing. cPN is associated with improved OS in patients with mRCC, although this effect is limited to patients with primary tumors <4 cm.

Keywords: Renal cell carcinoma; Neoplasm metastasis; Cytoreduction surgical procedures; outcomes; Survival analysis

1. Introduction

The treatment of metastatic renal cell carcinoma (mRCC) has undergone considerable advances in the last decade, most notably with the advent and widespread use of agents that target aberrant Von Hippel Lindau and hypoxia inducible factor pathways [1]. Prior prospective data demonstrating a survival advantage in patients who undergo cytoreductive radical nephrectomy (cRN) plus traditional immunotherapy, however, may not apply to most currently used systemic agents [2]. Consequently, a trend toward reduced usage of cRN, likely secondary to a lack of prospective evidence, has been documented [3,4]. As we await the results of ongoing prospective studies, several large retrospective series have provided evidence for a survival benefit to cRN in the targeted therapy era and, in

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turn, sparked renewed enthusiasm for cRN in select patient populations [5,6].

The role of cytoreductive partial nephrectomy (cPN) in the setting of mRCC, however, remains controversial. PN for localized kidney cancer, when technically feasible, is accepted as a standard over RN secondary to reduced long-term renal impairment and improved overall survival (OS) [7]. As targeted therapies and newer immunotherapies, such as nivolumab, offer extended life expectancies for patients with mRCC, surgical treatments should similarly focus on preservation of renal function in an effort to reduce cardiovascular morbidity and improve patients' ability to tolerate additional therapies. Currently, there exists a relative paucity of data examining the effects of cPN compared with cRN on OS.

In this study, we analyzed a large cohort of mRCC patients treated in the targeted therapy era with cytoreductive surgery (cPN or cRN). Our objective was 3-fold. First, we examined the use of cPN over time. Second, we identified predictors of utilization of cPN. Third, we performed a matched analysis of cPN and cRN in patients with mRCC and analyzed the effects on OS. We hypothesized that usage of cPN is increasing over time and that cPN is associated with a survival advantage over cRN in appropriately selected patients with smaller primary tumors.

2. Materials and methods

2.1. Data source

The National Cancer Database (NCDB) is a hospital registry-based database compiled from more than 1,500 Commission on Cancer accredited centers, and is sponsored jointly by the American College of Surgeons and the American Cancer Society. The NCDB captures more than 70% of newly diagnosed cancers in the United States and represents more than 34 million historical records [8].

2.2. Study population

Patients with a primary diagnosis of RCC were identified in the NCDB database (site code C649). Patients with metastases were identified as having clinical or pathologic M1 disease. Histology *included* clear cell (codes 8000, 8005, 8310, 8312, 8316, and 8959), chromophobe (codes 8050 and 8260), papillary (codes 8270, 8290, and 8317), sarcomatoid *component* (codes 8032, 8318, and 8963), and other variant histology (codes 8041, 8240, 8255, 8319, 8320, and 8323). Cytoreductive surgery was limited to PN (code 30) or RN (codes 40, 50, and 70). The study period selected was 2006 to 2013 to correspond with the approval of targeted therapies for treatment of metastatic disease. Patients with missing demographic, stage, or pathologic data were excluded (Fig. 1).

2.3. Study variables

Our independent variable of interest was type of cytoreductive surgery (cPN vs. cRN). Other covariates included patient specific demographics, such as age, gender, race, Charlson-Deyo comorbidity classification, insurance status, academic/research treatment facility, income, percentage without high school diploma, US region, and urban/metropolitan/rural residence status. Pathologic characteristics included tumor size (categorized as <4 cm, 4–7 cm, and >7 cm), histologic subtype (clear cell, chromophobe, papillary, sarcomatoid *component*, and other variants), grade (composite 1/2, 3/4, and unknown), concurrent metastasectomy, and surgical margin status. Systemic therapy was classified as no systemic therapy (none given), systemic therapy before surgery, after surgery, before and after surgery, and unknown sequence. Our dependent variable and primary outcome was OS.

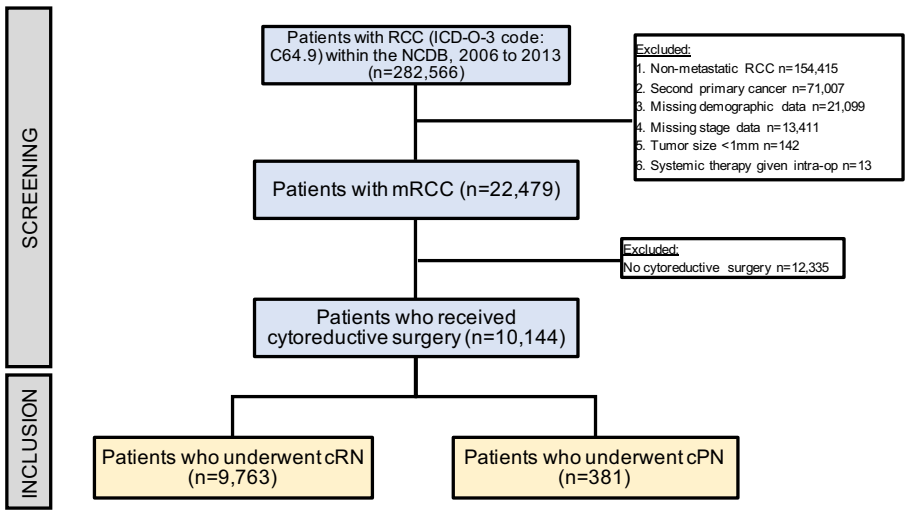

Fig. 1. CONSORT diagram of patient selection. ICD-O-3, International Classification of Diseases. (Color version of the figure available online)