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Clinical-Kidney cancer

The association between facility case volume and overall survival in patients with metastatic renal cell carcinoma in the targeted therapy era

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Abstract

Background: Improved overall survival of cancer patients treated by high-volume providers has been reported in surgical oncology and radiation oncology literature. Whether this volume-outcome association exists in medical oncology-managed metastatic solid tumors is uncertain. This study aimed to investigate the effect of facility case volume (FCV) on overall survival in patients with metastatic renal cell carcinoma (mRCC) diagnosed in the targeted therapy era.

Materials and methods: Adult patients diagnosed with mRCC between 2006 and 2015 were identified in the National Cancer Database. The primary exposure was FCV, which was defined by mRCC case volume of each treating facility. The association between FCV and all-cause mortality in mRCC was investigated in multivariable Cox regression model and validated with inverse propensity-score weighting method. Logistic regression was used to identify independent predictors for treatment at high-volume facilities. Covariates adjusted for were sociodemographics, tumor characteristics and treatment modalities.

Results: There were 31,329 mRCC patients identified. The mean follow-up time was 14.3 months. When FCV was coded as a continuous variable, each increment of 10 mRCC cases/y was associated with reduced all-cause mortality after baseline covariates adjustment [adjusted hazard ratio: 0.93, 95% confidence interval: 0.90−0.96, *P* value:<0.0001]. In dichotomized models, improved all-cause mortality was observed at cutoffs of 85th (4.3 cases/y), 90th (5.4 cases/y) and 95th (7.4 cases/y) but not at 50th (2.2 cases/y) and 75th (3.4 cases/y) percentiles. For illustrative purpose, 95th percentile was chosen and inverse propensity-score weighting-adjusted Kaplan−Meier curve demonstrated improved overall survival for mRCC patients treated at high-volume facilities (adjusted hazard ratio: 0.90, 95% confidence interval: 0.88−0.94, *P* value <0.0001; the 1-, 2-, 3-year survival rates were 41%, 26%, and 19% vs. 36%, 22%, and 16% for patients treated at high and low-volume facilities, respectively). Patients without insurance or with Medicaid status, with shorter travel distance, living in non-metropolitan area or in area with lower averaged education level were less likely to be treated at high-volume facilities.

Conclusions: Patients diagnosed with mRCC in the targeted therapy era have improved overall survival when treated at high mRCC-volume facilities, suggesting a volume-outcome association in medical oncology-managed metastatic solid tumors.

Keywords: mRCC; Hospital volume; Systemic therapy; Kidney cancer; Volume-outcome association

1. Introduction

Renal cell carcinoma (RCC) has an estimated 63,990 new cases and 14,400 deaths in 2017 [1]. While the RCC survival rate had been traditionally poor, the 5-year survival rate had increased from 57% in 1987 to 1989 to 74% in 2006 to 2012 [1]. This improvement is likely due to 2 main factors: first is the diffuse use of imaging studies which resulted in increased detection of early-stage disease [2,3]; the other is the targeted therapy (TT) era for advanced RCC beginning at the end of 2005 with 7 antiangiogenic drugs and 2 mammalian target of

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rapamycin inhibitors approved from 2005 to 2016 by the Food and Drug Administration [4]. Prior to the approval of nivolumab in November 2015 as second-line therapy for metastatic renal cell carcinoma (mRCC), the fundamental treatment for mRCC was TT with or without cytoreductive nephrectomy (CN) [5]. With such advancement in mRCC treatment since the end of 2005, the expertise of the treating facilities to keep up with new knowledge is essential in order to achieve the best patient outcomes.

In surgical oncology [6–12], there has been well-established evidence that surgical expertise improves with higher hospital/surgeon volume, which is reflected in decreased postoperative mortality [6,7], higher rate of achieving negative margins [8,10,13], a higher yield in lymph node dissection [8,10–13] and improved long term survival [6–12]. In radiation oncology [14–18], there is also emerging evidence demonstrating improved overall survival in patients treated at high-volume facilities. However, there are limited data whether this volume -outcome association exists in hematology-oncology managed cancers [19–22] especially in advanced solid tumors. Thus, the association between facility case volume (FCV) and overall survival (OS) in mRCC patients in the targeted therapy era was investigated. It was hypothesized that mRCC patients treated at high mRCC case volume facilities may have improved overall survival.

2. Methods

2.1. Data source

The National Cancer Database (NCDB) Participant Use Data File, which is a joint quality improvement program of the American College of Surgeons Commission on Cancer (CoC) and the American Cancer Society, was the data source for the present analysis. NCDB prospectively collects patient and facility characteristics. It captures 70% of newly diagnosed cancer cases in the United States [23] and is the largest cancer registry in the world. This study was exempted from review by Institutional Review Board.

2.2. mRCC cohort and FCV

Patients diagnosed with mRCC (site Code: C64.9; International Classification of Disease for Oncology Code 8000-8980) in 2006 to 2015 were identified. Metastatic status was determined with the 7th edition of the American Joint Committee on Cancer Stage Manual [24]. Because patients may receive treatment at multiple facilities, only patients treated at the reporting facility were included to estimate the effect of FCV on survival. FCV was defined by the averaged mRCC cases/year treated at each facility. Of note, facilities may not be CoC-accredited programs for every diagnosis year and thus may not contribute cases to NCDB during nonaccredited years. This current study followed prior recommendations published by Boffat et al. [23] for using NCDB: FCV of each facility was determined by summation of the mRCC cases contributed to NCDB and averaged by the number of years during which the facility was CoC-accredited instead of averaging over the study period. Sensitivity analysis was conducted using all stages of renal cell carcinoma (RCC) cases to define FCV.

2.3. Primary endpoint and covariates

The primary endpoint was to estimate the effect of FCV on OS in an mRCC cohort. Baseline covariates included age, sex, race, comorbidity status (captured by Charlson comorbidity score [25]: 0, 1, 2, ≥3), insurance status, distance to treating facility, year of diagnosis, and zip-code level sociodemographic factors (annual household income and percentage of residents without high school education were based on 2012 American Community Survey Data; residence type was categorized as metropolitan, rural and urban based on 2013 published data by the United States Agriculture Economic Research Service). Facility characteristics included facility type [academic/Research program (including National Cancer Institute-designated comprehensive cancer centers) were considered academic centers; community cancer program, comprehensive community cancer program, and integrated network cancer program were considered nonacademic] and facility location (grouped as Atlantic, New England, East Central, West Central, and West Pacific). Tumor factors included clinical tumor stage (T1, T2, T3, T4), clinical nodal stage (N0, N1), Fuhrman grade (1, 2, 3, 4) and histology type based on third edition of International Classification of Disease for Oncology as previously reported [26] (clear cell [8000, 8005, 8310, 8312-8316, 8359], chromophobe [8270, 8290, 8317], sarcomatoid [8032,8318, 8963], collecting duct [8319], papillary cell [8260], and other). NCDB collects first treatment course information. Treatment factors included receipt of TT, CN, metastasectomy and radiation. TT was reported in NCDB as single or multi-agent chemotherapy as published in prior studies [26,27]; CN was determined with the surgery of primary site codes (40, 50, 70); metastasectomy status was determined with variable “Surgical Procedure of Other Sites” which consists of surgery to regional/distant lymph nodes and distant sites. Radiation treatment was determined with variable “Radiation treatment volume”. All the above covariates were provided in NCDB Participant Use Data File [28].

2.4. Statistical analysis

Summary statistics were used to present baseline characteristics. Continuous variable was compared with Student *t* test and categorical variables were compared with Chi-square test. FCV was coded as a continuous variable. Multivariable Cox regression analysis was used to estimate the effect of FCV on all-cause mortality after baseline characteristics adjustment with the above mentioned variables. To explore the effect of FCV, dichotomized models with