Increasing Biopsy Utilization for Renal Cell Carcinoma Is Closely Associated With Treatment

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OBJECTIVE To describe recent temporal trends in biopsy use for renal cell carcinoma and to identify factors associated with biopsy.

MATERIALS AND METHODS Renal cell carcinoma diagnoses from 2003 to 2011 were identified using the National Cancer Data Base. Cases were classified by traditional (clinical stage T4, N1, or M1, or history of other malignancies) or expanded biopsy indications. Time trends were plotted, and multivariate analysis was performed to identify factors associated with biopsy.

RESULTS Of 171,406 eligible patients, we identified 21,019 patients (12.3%) who were biopsied. We observed a significant increase in biopsy usage with time for both the traditional (range, 16.7%-20.6%) and expanded (range, 6.9%-10.9%) subgroups ($P < .01$ for the trends). By the end of the study period, expanded indications accounted for most biopsies. By far, eventual treatment was the strongest factor associated with biopsy utilization for either subgroup. Compared with patients treated with partial nephrectomy, the odds of being biopsied were 2.7-4.3, 6.0-9.8, 14.6-23.0, and 3.0-4.4 times higher for patients managed with observation, cryoablation, radiofrequency ablation, or chemotherapy (including targeted therapy), respectively ($P < .01$). In the expanded-indications subgroup, other factors significantly associated with biopsy included sex, race, income, insurance, travel distance, case volume, region, and tumor size ($P < .01$ for all). Other significant factors in the traditional-indications subgroup were income, region, and Charlson score ($P < .01$ for all).

CONCLUSION In recent years, renal cell carcinoma biopsy has been increasingly used in patients with traditional and expanded indications. Its use is strongly associated with treatment and treatment-related factors. UROLOGY 86: 906–913, 2015. © 2015 Elsevier Inc.

Traditionally, renal mass biopsy was reserved for specific clinical scenarios—unresectable or metastatic renal cell carcinoma (RCC), nonrenal solid malignancy, lymphoma, or abscess—as a means to avoid unnecessary surgery.[1,2] This limited role was based on several historical factors, namely the perceived malignant potential of all renal masses, the convention of treating these masses surgically, the diagnostic inaccuracy of biopsy, and concerns over needle-track seeding.[3-6] Over the last 10-15 years, the indications for renal mass biopsy have expanded. This has occurred as a result of several changes, including the increased detection of incidental small renal masses, the recognition that these masses are frequently benign, the introduction of nonsurgical management options for localized disease and novel targeted therapies for advanced disease, and improvements in the diagnostic accuracy and safety of percutaneous biopsy.[7-13] As a result, biopsy has reemerged as an optional diagnostic tool in the evaluation of renal masses; however, it may be underutilized in current practice.[9,14] Although renal mass biopsy use showed signs of initial growth nearly a decade ago, its contemporary utilization, indications, and predictors are unclear.[15] Furthermore, the influence of treatment type on biopsy use has not been thoroughly investigated. We sought to better characterize biopsy utilization for RCC and explore factors associated with its uptake, in terms of its traditional and expanded indications.

MATERIALS AND METHODS

National Cancer Data Base (NCDB) Participant User File

The NCDB, a joint project of the American Cancer Society and the Commission on Cancer of the American College of Surgeons,

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is a comprehensive clinical oncology dataset that captures 70% of all incident malignancies in the United States. After institutional review board approval, we used the NCDB's participant user file for kidney and renal pelvis cancers.

Study Population

Using primary site coding from the *International Classification of Diseases for Oncology, Third Edition*, we identified 304,816 patients with RCC diagnosed from 2003 to 2011. Data prior to 2003 were excluded because comorbidity information was unavailable. Patients with T0 stage (0-cm tumor size) or unknown T stage were excluded given unclear significance and missing data (n = 115,197). For similar reasons, patients with unknown N or M stage were also excluded (n = 18,213).

Study Variables

Demographic, clinical, provider, and treatment variables were analyzed. Demographic factors included race/ethnicity, county, patient travel distance, educational level, income level, and insurance type. Race or ethnicity was categorized as non-Hispanic white, African-American, Hispanic, or other. County was categorized as urban, metropolitan, or rural based on data from the 2003 United States Department of Agriculture Research Service. Travel distance was grouped into tertiles based on the great-circle distance (in miles) between the patient's residence and the reporting hospital. Educational and household income levels were estimates based on 2000 United States Census data. Educational level (defined by the high school dropout rate) was categorized as highest (<14%), upper middle (14%-19.9%), lower middle (20%-28.9%), and lowest (≥29%). Income level (defined by annual income quartiles) was categorized as lowest (<$30,000), lower middle ($30,000-$35,000), middle ($35,000-$46,000), and upper middle (>$46,000). Insurance was labeled as uninsured, social (Medicare/Medicaid), and private or managed care. Clinical factors included age, sex, Charlson comorbidity index (CCI), other primary malignancies (no [RCC only] or yes), tumor size (<4 cm, 4-7 cm, 7-10 cm, or >10 cm), presence of bilateral tumors (no or yes), clinical T stage (1-4), clinical N stage (0 or 1), and clinical M stage (0 or 1). Age was grouped by decades (<55, 55-64, 65-74, or ≥75 years). CCI was calculated based on the *International Classification of Disease, Ninth Edition, Clinical Modification*, secondary diagnosis codes and categorized as 0 (no comorbidities), 1, or >1. Provider factors included hospital type, RCC case volume, and region. Using classifications designated by the Commission on Cancer, hospital types were defined as academic, comprehensive, community, or other. Hospitals were categorized into tertiles based on case volume, namely the total RCC diagnoses per hospital. Regions were based on the state of the reporting facility: Northeast, Midwest, South, and West. RCC treatments included radical nephrectomy, partial nephrectomy, observation, cryoablation, radiofrequency ablation, chemotherapy (including targeted therapies) immunotherapy, or radiotherapy.

Study Outcomes

Our primary end point was renal malignancy biopsy (RMB) utilization. Patients were divided into two subgroups based on the presence or absence of traditional indications for renal biopsy, that is, clinical evidence of locally advanced or metastatic disease (cT4 or cN1 or cM1) or history of other malignancies.

Statistical Analyses

Biopsy rates and total number of biopsies, for traditional and expanded indications, were plotted over time. Linear regression was applied to create trend lines, and the statistical significance of the trends was determined by the Cochran-Armitage test. Study variables were compared between biopsied and nonbiopsied groups using the Pearson chi-square test. The associations between the study variables and biopsy use were analyzed using multivariate logistic regression. The analysis was run separately for the traditional- and expanded-indications subgroups. Statistical tests were performed using SAS version 9.1 (SAS Institute Inc., Cary, NC). *P* values <.01 were considered statistically significant.

RESULTS

A total of 171,406 patients (mean age 62.7 ± 13.1 years, 61.4% male, 79.4% white) with predominantly localized RCC (71.9% cT1, 93.8% cN0, 89.3% cM0, 80.9% no other malignancies) met final inclusion criteria (Table 1). Of these, 52,459 (30.6%) patients (mean age 66.3 ± 12.2 years, 64.5% male, 81.2% white) had traditional indications for RMB (6.7% cT4, 20.4% cN1, 35.0% cM1, 62.5% other malignancies). Patients with traditional indications were more often managed nonoperatively (36.0% radical nephrectomy, 16.3% partial nephrectomy, 16.1% observation, 17.8% chemotherapy) vs those with expanded indications (59.6% radical nephrectomy, 27.3% partial nephrectomy, 5.4% observation, 1.3% chemotherapy); however, thermal ablation rates were similar in both cohorts (4.3%-4.5% cryoablation, 1.6%-1.7% radiofrequency ablation).

Between 2003 and 2011, 21,019 of 171,406 (12.3%) patients underwent RMB. Biopsy use increased over time, ranging from 10.0% to 13.9% ($P < .01$ for trend) (Fig. 1). The mean RMB rate was highest for clinical T3c (19.7%) and clinical T4 (25.4%) diseases. Over time, the RMB rate increased across all clinical T stages; however, this trend was only significant for T1 tumors, of which T1a tumors demonstrated the fastest rate of RMB growth (Fig. S1). Increasing biopsy use was seen both for patients with traditional and expanded biopsy indications. However, relative to patients with traditional indications, patients with expanded indications constituted a greater percentage of biopsies over time (Fig. 2). In 2011, 55% of biopsies were performed for expanded indications, compared with 48% at study onset. The odds of being biopsied for expanded indications were 1.2-1.4 times higher in 2009-2011 than in 2003 ($P < .01$). Alternatively, there was no significant difference in biopsy use for traditional indications during this time (Table 2).

On multivariate analysis, eventual treatment was the strongest factor associated with biopsy use (Table 2). Patients in the expanded-indications subgroup had 4.3 times higher odds of being biopsied if they were managed with observation rather than partial nephrectomy (odds ratio [OR] 4.32, confidence interval [CI] 3.95-4.71, $P < .01$). Similarly, this cohort had 9.8 and 23.0 times higher odds of biopsy if they underwent cryoablation or radiofrequency ablation, respectively ($P < .01$). Patients with larger tumors (>4 cm) were significantly less likely to undergo biopsy with 14%-51% decreased odds ($P < .01$). For patients in the