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Pathologic validation of renal cell carcinoma histology in the Surveillance, Epidemiology, and End Results program

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Abstract

Purpose: The Surveillance, Epidemiology, and End Results (SEER) program is an important epidemiologic research tool to study cancer. No information is available on its pathologic accuracy for renal cell carcinoma (RCC).

Methods: Central pathology review was analyzed as a part of the United States Kidney Cancer Study. Cases previously identified through the Detroit SEER registry were reviewed. The sensitivity and specificity, and positive and negative predictive values were calculated for each SEER-assigned subtype, with the central review assignments used as the reference.

Results: Of the 498 cases included in this study, 490 (98.5%) were confirmed to be RCC. The overall agreement for histology was 78.2% ($\kappa = 0.55$); however, individual cases were frequently reclassified. The sensitivity and specificity for SEER-assigned clear cell RCC were 79.1% and 88.1%, respectively, when based solely on the ICD-O-3 morphology code 8310 ($n = 310$), and 99.2% and 80.5% when 8312 (RCC not otherwise specified; $n = 41$) was also assumed to be clear cell. Although RCC not otherwise specified is frequently grouped with clear cell, only 78.1% had this histology. Assignments of papillary and chromophobe RCC had comparable sensitivities (73.5% and 72.4%, respectively) and specificities (97.5% and 97.6%). Positive predictive values for clear cell (excluding/including 8312), papillary, and chromophobe RCC were 95.5%/93.5%, 85.9%, and 65.6%, respectively.

Conclusions: Our findings confirm that nearly all RCC cases are correctly classified in SEER. The positive predictive value was higher for clear cell RCC than for papillary or chromophobe RCC, suggesting that pathologic confirmation may be warranted for studies of non–clear cell tumors. Published by Elsevier Inc.

Keywords: RCC; SEER; Histology; Pathology; Concordance; Accuracy

1. Introduction

In recent years, the urologic oncology community has utilized the Surveillance, Epidemiology, and End Results (SEER) program to better understand the etiology of renal cell carcinoma (RCC) and evaluate treatment strategies. The large number of patients included in SEER registries can be ideal for the studies of rare cancers or unusual subtypes. To ensure high quality, the SEER program implemented strenuous testing, including biannual case finding, recoding, and reliability studies in addition to educational and training programs [1]. Despite these efforts, pathology reporting practices may have a greater influence on data quality than variability in chart abstraction. According to SEER coding rules, cancer type and histology should be gathered primarily from the pathology or cytology report or both. Registry medical abstractors are also instructed to gather additional information from the medical records and

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operative reports. Although the College of American Pathology sets forth specific organ/cancer site guidelines for reporting, significant deficiencies in pathologic reporting exist [2,3]. SEER histology coding greatly depends on the pathologist, but currently, there is no method of pathologic data auditing.

In 2004, a study of lung cancer histology in SEER determined that an independent slide review may be required for the precise designation of histologic subtype [4]. Since then, no additional studies have assessed the accuracy of SEER pathology reporting. We set out to determine the accuracy of reporting of RCC histology in SEER compared with an independent pathologic review of cases included in the United States Kidney Cancer Study (USKC).

2. Methods

We utilized existing data from the USKC, a large case-control study that was conducted in Detroit, MI and Chicago, IL between February 2002 and January 2007 [5]. For the purposes of this analysis, USKC cases with reported ICD-O-3 histology in the Detroit SEER registry were selected for comparison with histologic classifications in a central pathology review. All available nephrectomy specimens had 1 to 3 of the most representative hematoxylin and eosin–stained slides sent to the National Cancer Institute for review by an expert kidney cancer pathologist (MM), who was blinded to SEER histology. In the central review, RCC histology was designated according to the Union Internationale Contre le Cancer/American Joint Committee on Cancer recommendations [6]. Although papillary renal tumors were broken into subtypes in this review, for our analysis, they were grouped together to compare to the SEER registry. The available tissue specimens were insufficient to appropriately identify histologic subtype for 32 cases, which were considered "unclassifiable" and excluded from all analyses. Lesions such as benign renal cysts, transitional cell carcinoma, or oncocytomas were considered "not RCC."

Patient demographics and tumor histology classifications in both SEER and the central pathology review were available for 498 cases. An agreement between reported histology in SEER and the central pathology review was analyzed overall and by individual histology. Central pathology review was considered the gold standard for the histologic classification. For each histologic type, we dichotomized cases (e.g., clear cell RCC vs. other) and calculated the percent agreement; sensitivity (e.g., the percentage of cases identified as clear cell RCC in the central pathology review that were correctly classified as such in SEER); specificity (e.g., the percentage of cases identified as non–clear cell RCC in the central review that were classified as non–clear cell in SEER); positive predictive value (PPV; e.g., the percentage of cases coded as clear cell RCC in SEER that were confirmed as such in the central pathology review); and negative predictive value (NPV; e.g., the percentage of cases coded as non–clear cell RCC in SEER that were confirmed as such in the central review). For each histologic type, the McNemar testing was used to check for differential misclassification.

Table 1
Patient demographic information ($n = 498$)[a]

Characteristic	*n*, %
Sex	
Female	222 (44.6)
Male	276 (55.4)
Race	
White	363 (72.9)
Black	135 (27.1)
Age at diagnosis	
<45	65 (13.1)
45–54	127 (25.5)
55–64	162 (32.5)
65–74	109 (21.9)
75+	35 (7.0)

[a]Excludes patients with "unclassifiable" RCC histology in the pathology review.

3. Results

Of the 498 cases included in this analysis, 490 (98.5%) were confirmed to be RCC in the central pathology review. Over half of the cases that were included were male (55.4%) and most were non-Hispanic whites (72.9%; Table 1). Table 2 demonstrates the distribution of confirmed RCC cases with classifiable histology in both SEER and the central pathology review ($n = 490$). According to SEER,

Table 2
RCC histologic subtypes in SEER and central pathology review ($n = 490$)[a]

Histology	SEER *n*, %	Pathology review *n*, %
Clear cell	310 (63.3)	372 (75.9)
Including *NOS*[b]	351[b] (71.6)	
Papillary	71 (14.5)	83 (16.9)
Chromophobe	32 (6.5)	29 (5.9)[c]
Other RCC	36 (7.4)[d]	6 (1.2)[e]
RCC NOS	41 (8.4)	–

[a]Excludes patients with non-RCC and "unclassifiable" RCC histology in the pathology review.

[b]Includes all 312 clear cell RCC cases and the 41 cases classified as RCC NOS (8312).

[c]Includes cases identified as either chromophobe or hybrid oncocytic neoplasms.

[d]Other in medical abstract data includes the following cases: 24 cyst-associated RCC (8316); 12 adenocarcinoma with mixed subtypes (8255); 2 collecting duct carcinoma (8319); and 2 granular cell carcinoma (8320).

[e]Other in central pathology review data includes the following cases: 4 multilocular cystic RCC; 1 collecting duct carcinoma; and 1 neuroendocrine tumor.