Combined Renal Sinus Fat and Perinephric Fat Renal Cell Carcinoma Invasion Has a Worse Prognosis Than Either Alone

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Abbreviations and Acronyms

MVI = microvascular invasion

PN = perinephric fat

RCC = renal cell carcinoma

RVI = renal vein invasion

SF = sinus fat

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Purpose: Recently groups reached differing conclusions when examining the prognostic significance of renal cell carcinoma perinephric and sinus fat invasion. We evaluated the impact of these pathological features on renal cell carcinoma survival and recurrence.

Materials and Methods: We identified the pathological and clinical records of 110 patients treated surgically for renal cell carcinoma with extrarenal extension at our institution between 1997 and 2007. Patients with von Hippel-Lindau disease were excluded from study. We used Kaplan-Meier survival curves with the log rank statistic to evaluate differences between groups. Cox logistic regression analysis was used to control for metastatic disease, tumor size and renal vein involvement to determine differences among the groups.

Results: Patients with perinephric plus sinus fat invasion had worse cancer specific survival than those with perinephric or sinus fat invasion alone ($p < 0.005$). There was no difference in cancer specific survival between those with sinus vs perinephric fat invasion ($p = 0.248$). On multivariate analysis perinephric plus sinus fat invasion was a significant prognostic factor for death from renal cell carcinoma compared to sinus fat invasion alone ($p = 0.038$).

Conclusions: Patients with combined renal sinus and perinephric fat invasion had a worse prognosis than those with either alone. Considerations should be made to stage these cases accordingly.

Key Words: kidney; carcinoma, renal cell; neoplasm invasiveness; adipose tissue; mortality

The American Joint Committee on Cancer TNM system is the most widely used RCC staging system. According to the most recent update in 2010 stage T3a includes invasion outside the kidney parenchyma but not through Gerota's fascia, and SF and renal vein involvement. It also includes invasion into renal SF and invasion through the renal capsule into PN. Previous studies suggested that renal sinus invasion is a possible route of metastatic spread.[1] The ample vascular and lymphatic supply in this area may serve as channels for dissemination. The remainder of the kidney is bound by a capsule that may serve as a barrier to extrarenal spread or metastasis. Due to the heterogeneous biological behavior of the T3 categorization investigators have examined recurrence and survival rates in this group, and proposed staging system modifications.[2,3] Groups have reported that adrenal invasion is associated with a worse prognosis than that of other T3 tumors and, thus, tumors with adrenal invasion should more properly be staged as T4.[4,5]

Recent studies show the prognostic significance of renal sinus invasion in more detail. A group from the Mayo Clinic reported that patients with renal

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SF invasion are more likely to die of RCC than those with PN invasion even when adjusting for metastatic disease.[6] Results from an M. D. Anderson Cancer Center RCC database contrasted with this report since in that cohort of 365 patients there was no difference in cancer specific survival among those with renal SF and/or PN invasion.[7]

Criticism of the current TNM staging system has focused on the T3 grouping with reports that tumor size is a more significant prognostic factor than isolated PN invasion.[8] This group has considerable outcome heterogeneity. Other investigators reported that patients with combined renal vein and PN invasion have a worse outcome than patients with either alone.[9] Groups have questioned whether renal capsule invasion is a significant prognostic factor.[10] Due to these conflicting reports we identified a cohort of patients with PN and/or SF invasion, and evaluated the impact of histological features on recurrence risk and RCC specific survival.

MATERIALS AND METHODS

All studies were done with University of Iowa institutional review board approval. Patients who underwent surgical extirpation for RCC at our institution between 1997 and 2007 were entered into a database. Those with pathologically confirmed renal sinus involvement or PN extension were identified. Patients with von Hippel-Lindau disease or adrenal invasion were excluded from analysis. The records of 110 patients who met these criteria were identified and studied. Variables analyzed were Fuhrman nuclear grades 1 to 4, tumor size by greatest dimension, necrosis or MVI, metastatic disease at surgery based on preoperative imaging and pathological reports, lymph node involvement and RVI. Patients with extension into but not through the renal capsule were not considered to have perinephric invasion.

Statistical analysis was done with SPSS®, version 16.0 and SigmaPlot® 11.0. Comparisons between groups were done using the t test or the Fisher exact statistic. For data analysis we used the Kaplan-Meier method for survival functions with the log rank statistic for comparison between groups. Cox proportional hazards regression analysis was used to examine prognostic variables, controlling for the most significant variables on univariate analysis.

RESULTS

Our cohort included 110 patients with a mean postoperative followup of 25.3 months (range 0 to 96.4), of whom 45 (40.9%) died of disease during followup. Cases were analyzed as 3 groups, including 41 (37.2%) of SF involvement only, 36 (32.7%) of PN invasion only and 33 (30.0%) of PN plus SF invasion. There were significant differences among the groups (table 1). Fewer patients with PN plus SF invasion had incidentally discovered tumors. Those with PN plus SF invasion were less likely to undergo laparoscopic surgery ($p = 0.041$) and they had larger tumors. Of patients with PN plus SF invasion 60% had clinical metastatic disease or positive lymph nodes at surgery compared to 22.2% in the PN and 24.4% in the SF groups. Those in the SF and PN plus SF groups also had a higher likelihood of RVI than that in patients with PN invasion alone.

Disease specific survival was significantly worse in the PN plus SF group than in the SF alone and the PN alone groups ($p < 0.001$ and < 0.005, respectively, part *A* of figure). We noted no significant difference in disease specific survival between the SF and PN groups ($p = 0.248$). When recurrence was used as an end point, again we noted a significant difference between patients with PN plus SF invasion vs that in patients with PN or SF invasion alone ($p < 0.003$, part *B* of figure).

Due to the significantly higher incidence of metastatic disease at surgery in the PN plus SF group we examined whether this difference could be responsible for worse disease specific survival. When patients with

Table 1. *Invasion group demographic and pathological characteristics*

				p Value		
	SF	PN	SF + PN	PN vs SF	PN + SF vs PN	PN + SF vs SF
Mean age	60.6	60.5	63.3	0.966	0.298	0.365
No. men (%)	22 (61.1)	31 (75.6)	20 (60.6)	0.220	0.210	1.0
No. white (%)	33 (91.7)	31 (75.6)	27 (81.8)	0.074	0.580	0.294
No. laparoscopic (%)	7 (19.4)	12 (30.0)	3 (9.1)	0.427	0.041	0.311
No. partial (%)	0	5 (12.5)	0	0.056	0.06	
No. incidental (%)	5 (13.9)	12 (29.3)	3 (9.1)	0.168	0.042	0.712
Mean tumor size (cm)	8.87	7.91	12.07	0.26	<0.001	0.007
No. metastasis (%)	8 (22.2)	10 (24.4)	20 (60.6)	1.0	0.002	0.002
No. high grade (3–4) (%)	19 (52.8)	28 (68.3)	28 (84.8)	0.24	0.11	0.005
No. RVI (%)	24 (66.7)	9 (21.9)	24 (72.7)	<0.001	<0.001	0.61
No. necrosis (%)	17 (47.2)	23 (56.1)	22 (66.7)	0.50	0.47	0.14
No. MVI (%)	18 (50.0)	19 (46.3)	22 (66.7)	0.82	0.10	0.22
No. clear cell Ca (%)	30 (83.3)	37 (90.2)	28 (87.5)	0.577	0.991	0.885