A Comparison of Radiographic and Morphometric Characteristics and Outcomes in T3a Pathologically Upstaged and Non-Upstaged Renal Cell Carcinoma

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Introduction

- A significant portion of patients presenting with clinically localized Renal Cell Carcinoma (Stage 1, 2) are pathologically upstaged to Stage 3 following surgical intervention.
- Improved detection of potential T3 upstaging may prompt changes in disease management which may impact patient survival
- Focused comparisons between pathologically upstaged T3a masses and non-upstaged T3a masses are seldom found.
- We sought to compare pathologically upstaged and non-upstaged T3a masses to identify characteristics of upstaged masses and predictors of T3a tumors and impact on oncological outcomes.

Methods

- We conducted a single center retrospective analysis of patients with pathologic T3a RCC who underwent surgical intervention.
- The cohort was divided into an upstaged group of patients with cT1-cT2/pT3a RCC and a non-upstaged group of patients with cT3a/pT3a RCC
- We sought to delineate proportion of under-diagnosed pT3a RCC, location of upstaged disease, and predictors for upstaging.
- Primary outcome was overall survival (OS), with secondary outcomes being recurrence-free survival (RFS) and cancer-specific survival (CSS).
- Multivariable logistic regression analyses (MVA) were performed for predictors of T3a disease and survival outcomes.
- Kaplan Meier survival analyses (KMA) were performed to compare recurrence and survival outcomes

Results

- We analyzed 185 patients, of which 120 (64.9%) were upstaged to pT3a and 65 (35.1%) were cT3a and non-upstaged.
- Upstaged masses were significant for smaller size (6.8 vs 8.2 cm, p=0.008), lower R.E.N.A.L score (8.7 vs 9.9, p<0.001), less hilar involvement (29.2% vs 86.2%, p<0.001), and increased exophyticity (41.7% vs 23.1%, p=0.011).
- Upstaged masses had significantly greater proportions of perirenal fat invasion (53.3% vs 33.8%, p=0.011), but significantly less renal venous system (44.2% vs 78.5%, p<0.001) and renal sinus fat invasion (35.8% vs 63.1%, p<0.001).
- R.E.N.A.L domains R (OR=2.30-2.49, p=0.037-0.042), E (OR=0.39-2.32, p=0.003-0.009), N (OR=4.35, p=0.008), L (OR=0.53-7.698, p=0.001-0.031), and h (OR=0.527-3.424, p=0.001-0.031) were independent predictors for at least one foci of pT3a disease
- MVA demonstrated that non-upstaged status was associated with increased incidence of recurrence (HR=2.012, p=0.043) but not cancer-specific mortality (HR=1.274, p=0.581).
- KMA noted that upstaged status was associated with improved RFS outcomes compared to non-upstaged status (80.8% vs 75.4%, p=0.002) but not CSS (84.2% vs 87.7%, p=0.233).

Table 1: Patient Demographics and Radiographic and Pathologic Findings

	Upstaged (n=120, 64.9%)	Non-Upstaged (n=65, 35.1%)	p-value
Age at Diagnosis, years (st.dev.)	61.2 (13.2)	65.1 (10.2)	**< 0.001**
Sex, n (%)			0.958
Male	78 (65.0%)	42 (64.6%)	
Female	42 (35.0%)	23 (35.4%)	
Ethnicity, n (%)			
White	64 (53.3%)	29 (44.6%)	0.258
Latino	44 (36.7%)	29 (44.6%)	0.291
Asian	3 (2.5%)	4 (6.2%)	0.214
African American	4 (3.3%)	0 (0%)	0.137
Other	4 (3.3%)	3 (4.6%)	0.663
Body Mass Index, kg/m2 (st.dev)	30.01 (6.22)	28.78 (5.75)	0.105
Charlson Comorbidity Index (CCI) at Diagnosis (st.dev)	4.2 (2.4)	5.6 (2.3)	**< 0.001**
Tumor Size, cm (st.dev)	6.78 (3.71)	8.16 (3.59)	**0.008**
Mean R.E.N.A.L Nephrometry Score (st.dev)	8.71 (3.72)	9.94 (3.60)	**< 0.001**
R domain, n (%)			
1, <4cm	24 (20%)	5 (7.7%)	**0.028**
2, 4-7cm	42 (35%)	23 (35.4%)	0.958
3, >7cm	54 (45%)	37 (56.9%)	0.121
E domain, n (%)			
1, >50% exophytic	50 (41.7%)	15 (23.1%)	**0.011**
2, <50% exophytic	55 (45.8%)	43 (66.2%)	**0.008**
3, entirely endophytic	15 (12.5%)	7 (10.8%)	0.728
N domain, n (%)			
1 >7cm from collecting system	16 (13.3%)	0 (0%)	**0.002**
2, 4-7cm from collecting system	32 (26.7%)	1 (1.5%)	**0.001**
3, <4cm from collecting system	72 (60.0%)	64 (98.5%)	**0.001**
L domain, n (%)			
1, entirely above/below polar line	16 (13.3%)	2 (3.1%)	**0.025**
2, crossing polar line	56 (46.7%)	27 (41.5%)	0.503
3, >50% across polar line, crossing axial renal midline, or entirely between polar lines	48 (40%)	36 (55.4%)	**0.045**
L h domain, n (%)			
Hilar tumor	35 (29.2%)	56 (86.2%)	**< 0.001**
Location of T3 disease, n (%) [a]			
Collecting system	6 (5%)	5 (7.7%)	0.460
Venous system	53 (44.2%)	51 (78.5%)	**< 0.001**
Perirenal fat	64 (53.3%)	22 (33.8%)	**0.011**
Renal sinus fat	43 (35.8%)	41 (63.1%)	**< 0.001**

Figure 1: Kaplan Meier Analysis for Recurrence-Free Survival and Cancer-Specific Survival

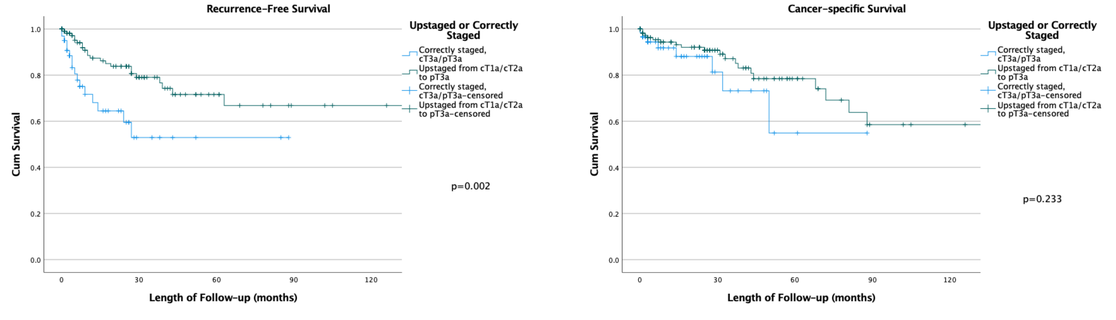

Table 2: Multivariate Analysis for Predictors of pT3a Disease Location

	Variable	OR	95% CI	p-value
Venous System Invasion (n=104)	Age (continuous)	1.022	0.833-1.192	0.443
	Sex (female vs male)	1.400	0.757-2.590	0.283
	R.E.N.A.L score (continuous)	1.175	0.722-1.346	0.319
	R domain (2+ vs 1)	2.301	1.018-4.627	**0.042**
	E domain (2+ vs 1)	1.405	0.765-2.579	0.272
	N domain (2+ vs 1)	4.348	1.346-14.043	**0.008**
	L domain (2+ vs 1)	2.178	0.804-5.897	0.119
	Hilar domain (hilar mass vs non-hilar mass)	3.200	1.742-5.877	**< 0.001**
	Surgery Method (radical vs partial)	1.784	0.968-3.291	0.073
	Tumor Histology (non clear cell vs clear cell)	0.751	0.333-1.694	0.489
Perirenal Fat Invasion (n=86)	Age (continuous)	0.882	0.494-1.574	0.378
	Sex (female vs male)	0.605	0.327-1.118	0.107
	R.E.N.A.L score (continuous)	0.781	0.421-1.253	0.255
	R domain (2+ vs 1)	0.612	0.274-1.315	0.278
	E domain (2+ vs 1)	0.389	0.209-0.723	**0.003**
	N domain (2+ vs 1)	0.490	0.170-1.410	0.179
	L domain (2+ vs 1)	0.299	0.102-0.876	**0.020**
	Hilar domain (hilar mass vs non-hilar mass)	0.527	0.293-0.947	**0.031**
	Surgery Method (radical vs partial)	0.976	0.532-1.792	0.939
	Tumor Histology (non clear cell vs clear cell)	1.278	0.573-2.854	0.548
Renal Sinus Fat Invasion (n=84)	Age (continuous)	0.815	0.586-1.128	0.148
	Sex (female vs male)	1.268	0.692-2.324	0.442
	R.E.N.A.L score (continuous)	1.576	0.811-2.914	0.102
	R domain (2+ vs 1)	2.494	1.042-5.969	**0.037**
	E domain (2+ vs 1)	2.316	1.232-4.354	**0.009**
	N domain (2+ vs 1)	1.931	0.643-5.798	0.234
	L domain (2+ vs 1)	7.698	2.185-12.116	**< 0.001**
	Hilar domain (hilar mass vs non-hilar mass)	3.424	1.867-6.282	**< 0.001**
	Surgery Method (radical/partial)	2.006	1.071-3.756	**0.031**
	Tumor Histology (non clear cell vs clear cell)	1.439	0.638-3.246	0.379

Table 3: Multivariate Analysis for Predictors of pT3a Disease Outcomes

	Variable	OR	95% CI	p-value
Recurrence (n=39)	Staging (non-upstaged vs upstaged)	2.012	1.022-3.960	**0.043**
	E domain (2+ vs 1)	2.412	1.080-5.388	**0.032**
	N domain (2+ vs 1)	1.889	0.433-8.241	0.398
	Margin status (positive vs negative)	1.889	0.901-4.780	0.087
Cancer-Specific Mortality (n=27)	Staging (non-upstaged vs upstaged)	1.274	0.539-3.010	0.581
	E domain (2+ vs 1)	3.151	1.158-8.569	**0.025**
	Margin status (positive vs negative)	2.856	1.014-6.348	**0.049**

Conclusion

- Pathologically upstaged T3a RCC was associated with different morphology and invasion patterns when compared to non-upstaged T3a masses.
- Pathologically upstaged T3a RCC had higher recurrence-free survival outcomes compared to non-upstaged T3a RCC, but there were no differences in cancer-specific mortality outcomes
- R.E.N.A.L domains can be useful in identifying masses with upstaging potential and predicting their location of invasion and may aid in preoperative planning and risk stratification.