Characterization of Cystic Renal Cell Carcinoma

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Abstract

Background: Bosniak classification of renal cysts provides radiographic prediction of malignant histology but does not address tumor aggressiveness. Limited evidence suggests cystic renal cell carcinoma (RCC) tumors may be indolent, challenging whether resection is routinely warranted, however oncologic outcomes remain poorly characterized. Here we provide the largest study to our knowledge characterizing tumor histology and metastasis rates for cystic RCC patients, while identifying radiographic features predicting aggressive biology.

Methods: Cross-sectional imaging was reviewed for 864 consecutive RCC patients undergoing partial or radical nephrectomy at a single National Comprehensive Cancer Network cancer center from 2006-2013. Patients with cystic RCC tumors defined as ≥70% cystic (solid composition ≤30%) were identified. For each, an estimated solid volume (ESV) score was calculated as the product of tumor volume ($^4/_3\pi\,r^3$) and radiographically estimated solid percentage (0-30%); the solid component was further classified as hypo- (<40 net HU) vs. hyperenhancing (>40 net HU). Cyst features were correlated with high grade histology and postoperative metastasis.

Results: 50 cystic RCC lesions from 49 patients were identified. Median solid percentage was 10% and median ESV score was 5 cc (range 0-595 cc). Histologic subtypes included 32 clear cell, 17 papillary and 1 unclassified. 13 (26%) tumors had high grade histology. With a median follow up of 24 months, 6 (12%) patients developed metastasis. High grade and/or metastatic cases (N=14) could be split into two groups: 1) hyperenhancing/clear cell RCC with a high ESV score, 2) hypoenchancing/papillary or unclassified RCC. Among cysts with hyperenhancement (all clear cell RCC), a threshold ESV of ≥70 cc was 100% sensitive and 83% specific for high grade and/or metastasis. In contrast, cysts with solid hypoenhancement (all papillary or unclassified RCC) were frequently associated with high grade histology and metastasis at even low ESV scores (range 3-108 cc).
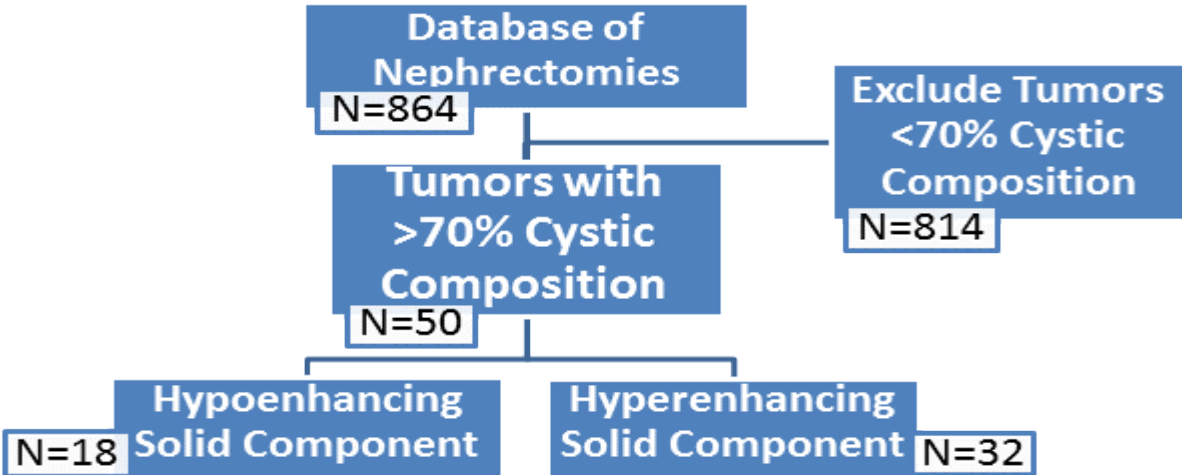
Conclusions: ESV score and enhancement level can help identify aggressive variants of cystic RCC. Hyperenhancement indicates clear cell histology and suggests indolent biology when ESV is low. Conversely, cystic RCC with solid hypoenhancement suggests papillary histology which may be aggressive even with low ESV. Surgery is advisable for lesions with high ESV and for all hypoenhancing cystic RCC lesions regardless of ESV, while hyperenhancing cystic lesions with low ESV may be good surveillance candidates.

Introduction

- Renal cell carcinoma (RCC) is diagnosed annually in 64,000 U.S. individuals and continues to increase.
- Bosniak's renal cyst classification has been the primary tool for predicting RCC in renal cysts but does not predict RCC aggressiveness or metastatic potential.
- Mounting evidence supports certain low risk RCC lesions can be safely surveyed without resection, however the oncologic risk of cystic RCC is unknown due to scant characterization of oncologic outcomes.
- We sought to characterize the histologic grade and metastatic potential of cystic RCC patients, while identifying radiographic features predicting aggressive biology.

Methods

- Retrospective review of 864 consecutive RCC patients undergoing partial or radical nephrectomy between 2006-2013 at our institution.
- Radiographic imaging for all patients reviewed to identify RCC tumors with ≥70% cystic component (≤30% solid component):

Database of Nephrectomies N=864 → Exclude Tumors <70% Cystic Composition N=814

Tumors with >70% Cystic Composition N=50 → Hypoenhancing Solid Component N=18 / Hyperenhancing Solid Component N=32

- Cyst features were radiographically measured, including Bosniak grade, RENAL score, tumor volume ($^4/_3\pi r^3$) and solid component percentage and degree of enhancement.
- Solid hyperenhancement defined as >40 net hounsfield units (HU); solid hypoenhancement defined as <40 net HU.
- Estimated Solid Volume (ESV) score was calculated as the product of tumor volume and solid percentage (0-30%).

Table 1. Patient Features

Tumor Grade:	Low	High
n =	36 (73%)	13 (27%)
Median Age	61	62
Gender		
Male (n=)	26 (53%)	12 (24%)
Female (n=)	11 (22%)	1 (2%)
Race		
White (n=)	32 (65%)	12 (24%)
Black (n=)	4 (8%)	1 (2%)
Other	1 (2%)	0
BMI		
< 35 (n=)	33 (67%)	12 (24%)
≥ 35 (n=)	4 (8%)	1 (2%)

Tumor Grade:	Low	High
Median RENAL Score	8	10
Bosniak Grade		
3 (n=)	10	0
4 (n=)	27	13
Median Solid %	10	15
Median Size (cm)	2.1	4.8
Median Volume (cc)	22.9	387
Median SVS (cc)	2.7	58.4
Hyper-enhancing (n=)	28 (58%)	4 (8%)
Hypo-enhancing (n=)	9 (18%)	8 (16%)

Table 2. Perioperative Features

	Total
Mean **EBL** (mL)	315
Mean **ASA PS**	2.2
Kidney Function (Δ eGFR)	-10.6
Surgery Type	
Partial (n=)	33 (66%)
Radical (n=)	17 (34%)
Laterality	
Left (n=)	26 (52%)
Right (n=)	24 (48%)

Table 3. Oncologic Outcomes

Tumor Grade:	Low	High
pT stage:		
pT1a	24 (48%)	1 (2%)
pT1b	6 (12%)	3 (6%)
pT2a	4 (4%)	3 (6%)
pT2b	1 (2%)	3 (6%)
pT3	1 (2%)	2 (4%)
pT4	0	1 (2%)
pTx	1 (2%)	0
Histologic subtype:		
Clear Cell	26 (53%)	4 (8%)
Clear Cell, papillary variant	2 (4%)	0
Papillary	9 (18%)	8 (16%)
Unclassified	0	1 (2%)
Median follow up (months)	24	18
Metastasis	1 (2%)	5 (10%)
Local recurrence	0	1 (2%)

Results

- 50 cystic RCC lesions were identified in 49 patients
- Median solid percentage was 10%, median ESV score was 5 cc (range 0-595 cc).
- With a median follow up of 24 months, 6 (12%) patients developed metastasis.
- High grade and/or metastatic cases (N=14) could be split into two groups:
  1) Hyperenhancing/clear cell RCC with a high ESV score
  2) Hypoenhancing/papillary or unclassified RCC
- Among cysts with solid hyperenhancement (all clear cell RCC), a threshold ESV of ≥70 cc was 100% sensitive and 83% specific for high grade and/or metastasis.
- In contrast, cysts with solid hypoenhancement (all papillary or unclassified RCC) were frequently associated with high grade histology and metastasis even at low ESV scores (range 3-108 cc).

Figure 1. ESV score ≥70 Reliably Predicts Aggressive Biology of Hyperenhancing (Red) but not Hypoenhancing (Blue) Cystic RCC

Legend: Low Grade, Non-Metastatic; High Grade and/or Metastatic*. ESV = 595 cc. Y-axis: Solid Volume Score (cc). X-axis: Hyperenhancing (clear cell) / Hypoenhancing (papillary or unclassified)
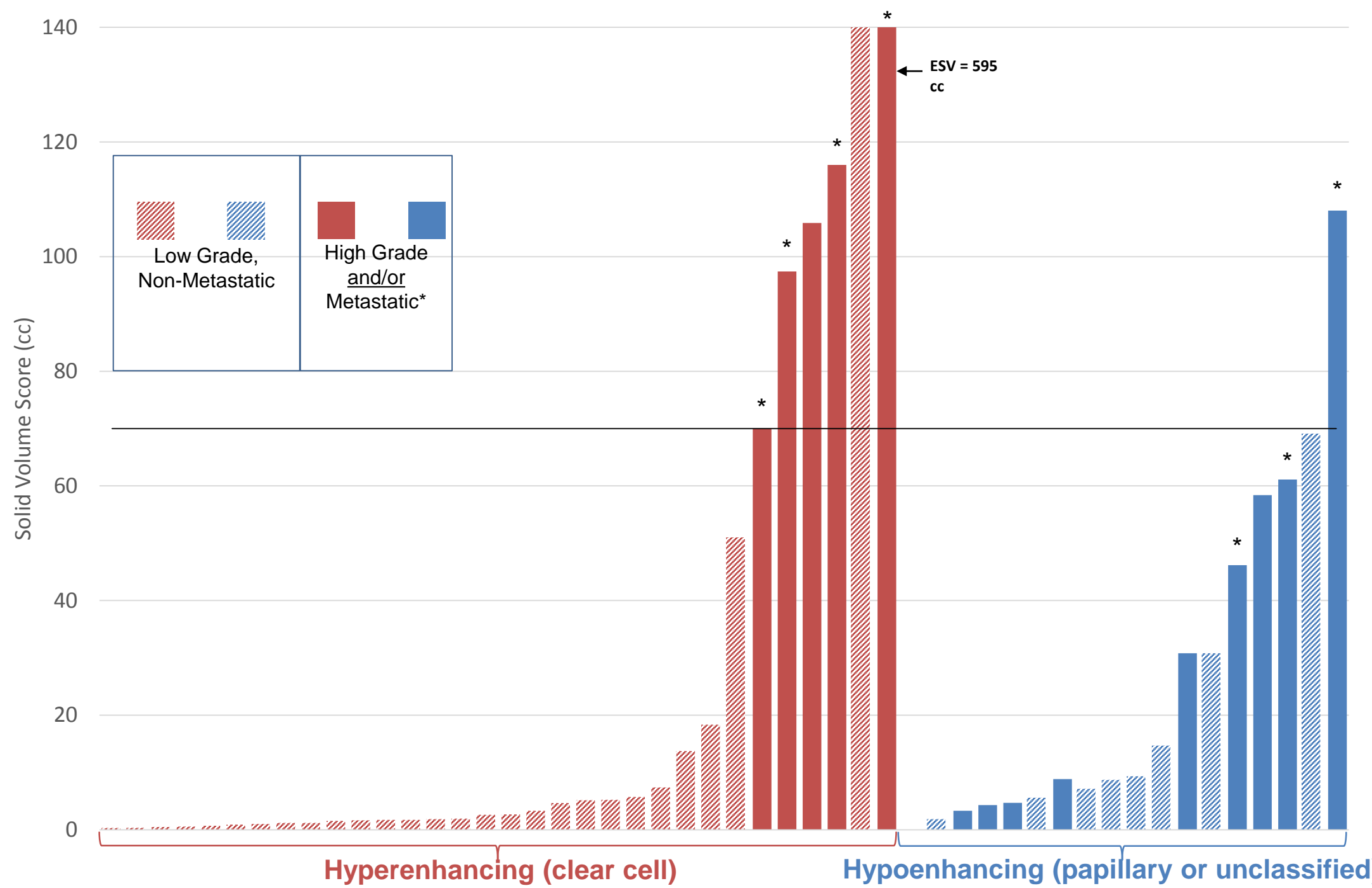
Conclusion

- ESV score and cyst enhancement together reliably identify clinically aggressive cystic RCC lesions
- Cystic RCC with hyperenhancement suggests clear cell histology and is indolent with low ESV
- Conversely, Cystic RCC with solid hypoenhancement suggests papillary histology, which may be aggressive even with low ESV
- Surgery is advisable for:
  - hyperenhancing cystic lesions with elevated ESV
  - hypoenhancing cystic RCC lesions regardless of ESV
- Surveillance can be considered for hyperenhancing cystic RCC with low ESV