Abstract #747

Renal Biopsy Cell Cycle Proliferation (CCP) Score Predicts Adverse Surgical Pathology in Renal Cell Carcinoma

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ABSTRACT

Background: The role of renal mass biopsy (RMB) in risk stratifying patients with renal cell carcinoma (RCC) is unclear. We sought to determine whether the cell cycle proliferation (CCP) score from RMB can improve risk stratification of localized RCC.
Methods: We identified patients with RCC who underwent RMB and subsequent partial/radical nephrectomy from 2000-2014. We used multivariable logistic regression to determine the association of patient-level variables and biopsy CCP score with adverse surgical pathology (Fuhrman grade 3-4, pT stage≥3, papillary type II histology, or evidence of metastasis at surgery). Effect size was estimated with odds ratios (OR) and discriminative performance with AUC.
Results: Overall, 94 of 202 patients (46%) had adverse surgical pathology. On multivariable analysis, CCP score >0 was associated with 2.38-fold increased odds of adverse pathology (Table). Relative to the model omitting CCP score (AUC=0.70), the addition of CCP score as a continuous (AUC=0.731) or binary (AUC=0.730) variable yielded increased discriminative performance. Similar associations were observed in an analysis limited to patients with low-grade tumors on biopsy (bCCP: OR 2.44, p=0.024; cCCP: OR 1.57, p=0.11). In both models, increased lesion size on imaging was consistently associated with adverse pathology.
Conclusions: Among patients with RCC, biopsy CCP score >0 was independently associated with adverse pathology, suggesting this classifier provides prognostic information beyond conventional pathologic data. Biopsy CCP score could be used to better guide patient-specific management.

BACKGROUND

- Management of localized renal masses has evolved in recent years, with active surveillance (AS) emerging as a viable option for smaller masses. There are limited tools available to discern which patients are optimal candidates for AS.
- Renal mass biopsy has been used to better risk stratify localized RCC. Yet there is poor grade concordance from renal biopsy to surgical pathology, and the possibility of misclassifying high-grade tumors as low-grade, often due to sampling error of heterogeneous tumors, is worrisome.
- Tissue-based molecular classifiers are used in risk stratification of several cancers. We sought to assess whether CCP score from renal mass biopsy could improve pre-operative risk stratification.

METHODS

- We identified patients with RCC (clear cell, papillary, or chromophobe) who underwent renal mass biopsy followed by partial/radical nephrectomy at the University of Michigan (UM) or Massachusetts General Hospital (MGH) from 2000-2014.
- Exclusion: sarcomatoid variants; neoadjuvant therapy; clinical evidence of bilateral, node-positive, or metastatic disease.
- The primary outcome was adverse surgical pathology, defined as: Fuhrman grade 3-4, pT stage≥3, papillary type II histology, or evidence of metastasis at surgery.
- To determine the impact of CCP score on fitted models, CCP score was added to a baseline multivariable model as i) a binary variable (CCP score >0) and ii) a continuous variable. Area under the receiver operating characteristic curve (AUC) quantified model performance.
- Subgroup analyses assessed CCP score in patients with low-grade tumors on biopsy (n=175) likely to benefit from additional testing and compared biopsy CCP vs. nephrectomy CCP in the subgroup with nephrectomy CCP score available (n=67).

RESULTS

- Of 202 patients in the study population, 94 (47%) had adverse pathology.

Table 1. Cohort characteristics by study site

All values: median (IQR) or N (%)	Overall (n=202)	MGH (n=97)	UM (n=105)
Age (yrs)	61 (53-68)	59 (51-68)	63 (53-70)
Male sex	129 (64%)	64 (66%)	65 (62%)
Non-white race	26 (13%)	11 (11%)	15 (14%)
Lesion size (cm)	3.20 (2.3-4.5)	2.90 (2.1-4.2)	3.80 (2.5-4.9)
Biopsy clear cell	142 (70%)	56 (58%)	86 (82%)
Biopsy grade 1	39 (19%)	33 (34%)	6 (6%)
2	136 (67%)	54 (56%)	82 (78%)
3	25 (12%)	9 (9%)	16 (15%)
4	2 (1%)	1 (1%)	1 (1%)
Biopsy CCP	0.10 (-0.39-0.56)	-0.10 (-0.51-0.28)	0.30 (-0.33-0.69)
Adverse pathology	94 (47%)	32 (33%)	62 (59%)
Grade 3-4	75 (37%)	20 (21%)	55 (52%)
pT stage≥3	43 (21%)	16 (16%)	27 (26%)
Papillary type II	8 (4%)	6 (6%)	2 (2%)
M1 at surgery	11 (5%)	8 (8%)	3 (3%)

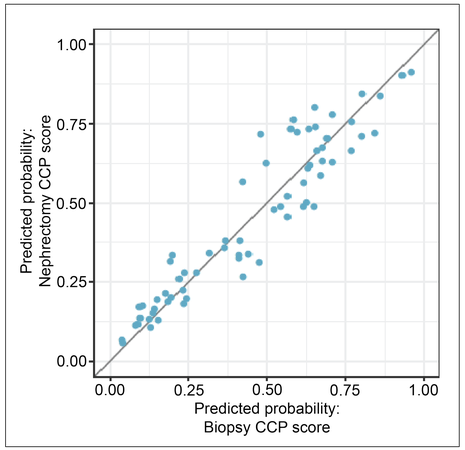

Figure 1. Predicted probabilities of adverse pathology in MV models including biopsy CCP score (x-axis) and nephrectomy CCP score (y-axis).

Table 2. Multivariable Logistic Regression for Adverse Surgical Pathology

Total (n=202)	Model 1: CCP omitted	Model 2: Binary CCP	Model 3: Cont. CCP
	OR (95% CI; p-value)	OR (95% CI; p-value)	OR (95% CI; p-value)
Age (per 1 year)	1.02 (1.00-1.05; 0.10)	1.03 (1.00-1.05; 0.055)	1.02 (1.00-1.05; 0.08)
Male sex	1.97 (1.04-3.82; 0.04)	1.80 (0.94-3.53; 0.08)	1.86 (0.97-3.63; 0.06)
Non-white race	1.30 (0.53-3.178; 0.56)	1.33 (0.54-3.26; 0.53)	1.33 (0.54-3.25; 0.52)
Mass size (per 1 cm)	1.33 (1.14-1.57; <0.001)	1.34 (1.15-1.60; <0.001)	1.32 (1.14-1.57; 0.001)
Bx clear cell	0.78 (0.39-1.53; 0.47)	0.49 (0.22-1.08; 0.08)	0.53 (0.24-1.16; 0.11)
Bx grade (1, 2, 3-4)	1.96 (1.12-3.53; 0.02)	1.77 (0.99-3.24; 0.06)	1.80 (1.02-3.28; 0.05)
Bx CCP >0 (vs ≤0)	-	2.38 (1.16-5.04; 0.02)	-
Bx CCP (per 1 unit)	-	-	1.66 (1.0-2.80; 0.05)
Model AUC	0.70	0.73	0.73

✔ Biopsy CCP score>0 was associated with more than two-fold increased odds of adverse pathology (Table 2).

✔ Addition of CCP score to multivariable models as a binary (AUC 0.73) or continuous (0.73) variable yielded improved classification relative to the baseline model omitting CCP score (0.70).

✔ Findings were consistent when analysis was restricted to patients with low-grade tumor on biopsy (n=175) most likely to benefit from additional testing in this setting.

✔ Biopsy- and nephrectomy-based CCP scores were well correlated; Pearson correlation = 0.55 (Figure 1).

✔ The adjusted model based on biopsy CCP score had a slightly higher AUC (0.72) than the model based on nephrectomy CCP score (0.69) after ten-fold cross-validation.

CONCLUSIONS

- CCP score determined from renal mass biopsy appears to provide prognostic information independent of other clinical variables such as tumor size and biopsy tumor grade. These findings were consistent in patients with low-grade tumor on biopsy.
- Performance of biopsy-based CCP score was slightly better than nephrectomy-based CCP score, suggesting that tumor heterogeneity and limited sampling of small renal masses may not preclude the use of tissue-based markers.
- These findings suggest that CCP score determined from renal tumor biopsy could be useful for risk stratification of localized RCC and support prospective evaluation of CCP score to confirm clinical validity and determine clinical utility.

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