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

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Disclosures

- No personal disclosures

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Background

- There is increasing recognition that many small renal cell carcinomas (RCC) do not require intervention and can instead be monitored with active surveillance
- Renal mass biopsy (RMB) is often performed in small renal masses to distinguish malignant from benign lesions and to better risk-stratify malignant disease
- The role of biopsy in risk-stratifying patients with localized RCC is limited by poor correlation between biopsy findings and final pathologic grade
- Tissue-based genetic classifiers may provide additional information in this setting

Background

- Previous data suggest the cell cycle proliferation (CCP) score obtained from nephrectomy specimens is associated with cancer recurrence during follow-up

Platinum Priority – Kidney Cancer
Editorial by A. Ari Hakimi and Martin H. Voss on pp. 770–771 of this issue

A Multigene Signature Based on Cell Cycle Proliferation Improves Prediction of Mortality Within 5 Yr of Radical Nephrectomy for Renal Cell Carcinoma

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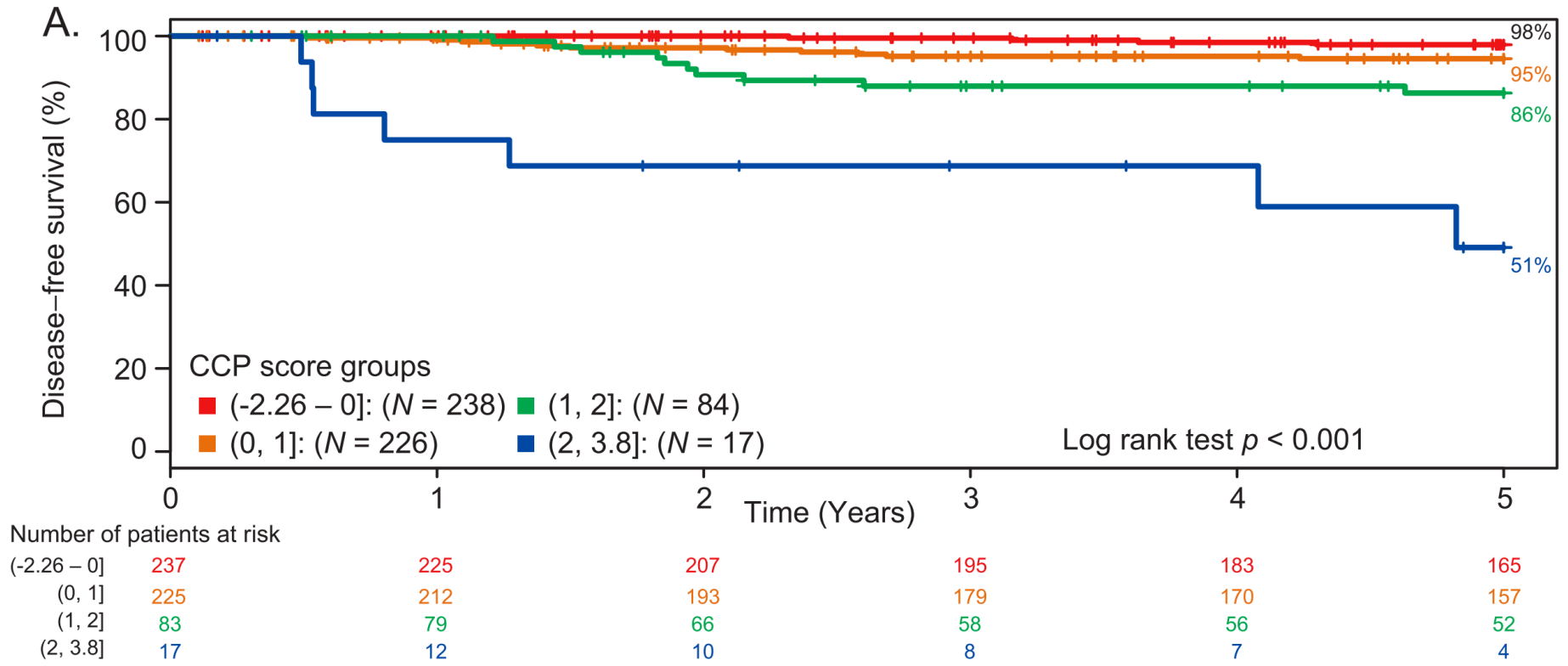


Objective

- Determine whether CCP score obtained in renal tumor biopsy tissue can improve risk stratification in patients with localized RCC

Methods

- Setting: University of Michigan (UM) and Massachusetts General Hospital (MGH) from 2000-2014
- Cohort: Patients with RCC who underwent RMB and subsequent partial or radical nephrectomy
- Outcome: Adverse pathology (AP) at nephrectomy
  - Fuhrman grade 3-4
  - Pathologic T stage ≥ 3
  - Papillary type II histology
  - Evidence of nodal or distant metastasis

Methods

- Baseline characteristics compared in subjects who did and did not have adverse surgical pathology
- Logistic regression performed to determine the association of age, sex, histology, grade, and biopsy CCP score with adverse surgical pathology
- Factors demonstrating a significant association ($p<0.05$) on univariable analysis were included in a multivariable model

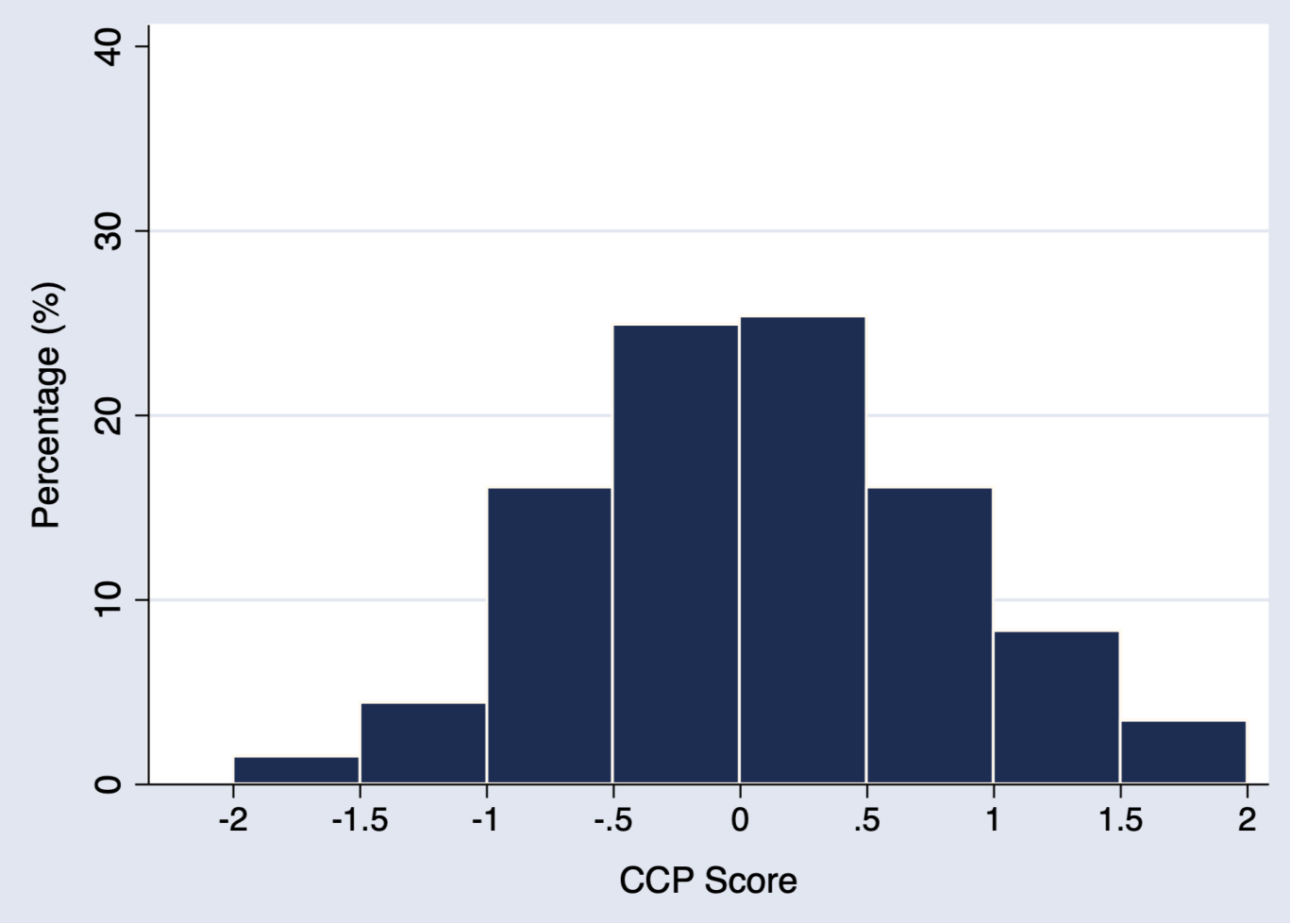
Results

- n=205 subjects
- n=95 with adverse pathology (46%)

Results: Study Cohort

	Overall (n=205)	No AP (n=110)	AP (n=95)	P-value
Age	61.0	59.7	64.7	0.008
Male sex	130 (64)	60 (55)	70 (74)	0.005
Clear cell bx	144 (70)	77 (70)	67 (71)	0.9
Biopsy grade				<0.001
Ungraded	73 (36)	49 (45)	24 (25)	
Low (1-2)	113 (55)	60 (55)	53 (56)	
High (3-4)	19 (9)	1 (1)	18 (19)	
CCP score	0.09	-0.09	0.30	0.01

Results: CCP Score



Median	0.09
IQR	-0.39, 0.55
Range	-1.57, 1.90
Mean	0.08
SD	0.72

Results: Multivariable Regression

	Multivariable OR (95% CI)	P-value
Age	1.03 (1.00-1.06)	0.054
Male sex	2.57 (1.33-4.99)	0.005
Biopsy grade Ungraded Low (1-2) High (3-4)	 0.64 (0.33-1.22) 1.00 (reference) 21.8 (2.66-179)	 0.18 0.004
CCP score ≥ 0.10	1.87 (1.01-3.47)	0.048

Results: Multivariable Regression

- Excluding 19 subjects with high-grade biopsy (n=186)

	Multivariable OR (95% CI)	P-value
Age	1.03 (1.00-1.06)	0.03
Male sex	2.47 (1.26-4.81)	0.008
Biopsy grade Ungraded Low (1-2)	 0.65 (0.34-1.24) 1.00 (reference)	0.2
CCP score ≥ 0.10	1.95 (1.04-3.65)	0.038

Discussion

- In a multivariable model including age, sex, and biopsy pathology, increased CCP score was independently associated with nearly two-fold increased risk of adverse surgical pathology

- This association increased in magnitude and significance when considering only those patients with low-grade or ungraded tumors

- While most patients with high-grade biopsy pathology will proceed to definitive treatment, the information provided by the CCP score may be particularly useful in those with low-grade or ungraded cancers

Limitations

- Current model does not account for radiologic size
- Adverse pathology is a surrogate endpoint that may not accurately represent longer-term oncologic outcomes
- Study design does not assess or account for intratumoral heterogeneity

Conclusions

- CCP score obtained at renal biopsy appears to provide prognostic information beyond that of traditional clinicopathologic factors

- Additional data are needed to confirm these findings and identify optimal clinical settings for use

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