60. Kidney

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Emerging Prognostic Factors for Clinical Care

Gene Expression of the Primary Tumor

Over the past several years, techniques to incorporate tumor gene expression have been applied to patients with localized RCC who undergo nephrectomy. These gene expression results have then been incorporated into known prognostic variables and have been shown to add value in terms of prognostication. Although none are in routine clinical use presently, with broader availability and application of gene expression techniques, further refinement of prognostic schema may occur.

One approach examined 48 clear cell RCC samples by unsupervised clustering of gene expression data to reveal two distinct subsets, designated ccA and ccB.[1] These independent tumor types were confirmed in an independent cohort of 177 clear cell RCC tumors and shown to be significantly associated with different cancer-specific and overall survival. These associations with survival were of borderline significance (p = 0.089) when accounting for stage, grade, and performance status.

Another dataset looked at gene expression in 942 resected Stage I–III clear cell RCC primary tumors and developed a score based on gene expression (in 11 cancer-related and 5 reference genes), which was validated in 626 separate primary renal tumors.[2] In multivariable analysis accounting for known prognostic factors, this recurrence score was significantly associated with risk of tumor recurrence and overall survival (p < 0.0001).

Risk Assessment Models

The American Joint Committee on Cancer (AJCC) recently has established guidelines that will be used to evaluate published statistical prediction models for the purpose of granting endorsement for clinical use.[3] Although this is a monumental step toward the goal of precision medicine, this work was published only very recently. For this reason, existing models that have been published or may be in clinical use have not yet been evaluated for this cancer site by the Precision Medicine core of the AJCC. In the future, the statistical prediction models for this cancer site will be evaluated, and those that meet all AJCC criteria will be endorsed.

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Recommendations for Clinical Trial Stratification

Clinical trials tend to be focused on patients with high-risk localized disease for which the TNM staging system and the prognostic variables, especially histologic subtype, become important clinical trial stratification or selection features. In patients with metastatic disease, prognosis remains poor. Important additional considerations for patient selection and stratification in the design of clinical trials for these patients include prior therapy, performance status, metastatic burden, distribution of metastatic disease, and presence of anemia, thrombocytosis, neutrophilia, hypercalcemia, and elevated LDH.

Bibliography

1. Brannon AR, Reddy A, Seiler M, et al. Molecular Stratification of Clear Cell Renal Cell Carcinoma by Consensus Clustering Reveals Distinct Subtypes and Survival Patterns. *Genes & cancer.* 2010;1(2):152-163.
2. Rini B, Goddard A, Knezevic D, et al. A 16-gene assay to predict recurrence after surgery in localised renal cell carcinoma: development and validation studies. *The lancet oncology.* 2015;16(6):676-685.
3. Kattan MW, Hess KR, Amin MB, et al. American Joint Committee on Cancer acceptance criteria for inclusion of risk models for individualized prognosis in the practice of precision medicine. *CA: a cancer journal for clinicians.* 2016.