69

The UCLA histo-genetic risk classification (U-HGRC) to stratify prognosis of localized clear-cell renal cell carcinoma

Eur Urol Suppl 2019; 18(1);e92

Lebacle C. [1], Pooli A. [2], Rao N. [3], Wood E.L. [4], Kroeger N. [5], Kim G. [6], Faiena I. [2], Liu S.T. [7], Chamie K. [2], Belldegrun A.S. [2], Shuch B. [2], Drakaki A. [8], Pantuck A.J. [2]

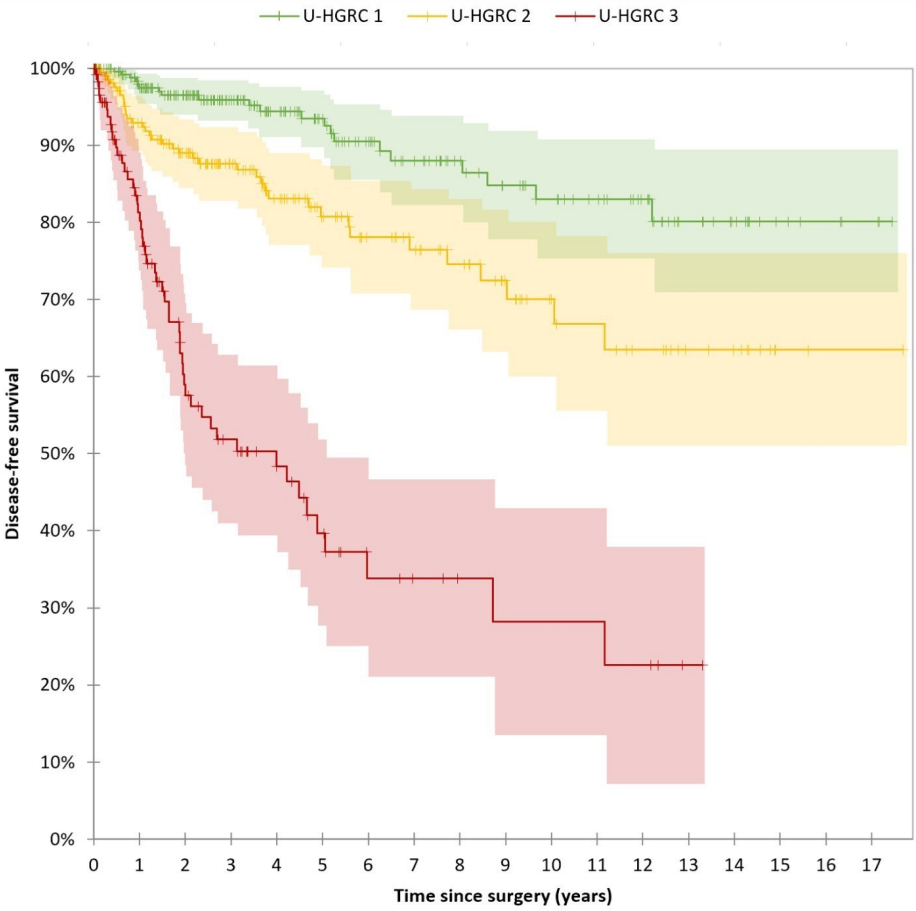
[1]Institute of Urologic Oncology (IUO), David Geffen School of Medicine at UCLA, Los Angeles, CA - Department of Urology, University Hospital Bicetre, APHP, University Paris-Saclay, Dept. of Urology, Le Kremlin Bicetre, France, [2]Institute of Urologic Oncology (IUO), David Geffen School of Medicine at UCLA, Dept. of Urology, Los Angeles, United States of America, [3]David Geffen School of Medicine at UCLA, Dept. of Pathology and Cytogenetic lab, Los Angeles, United States of America, [4]David Geffen School of Medicine at UCLA, Dept. of Urology, Los Angeles, United States of America, [5]University Medicine Greifswald, Dept. of Urology, Greifswald, Germany, [6]Fielding School of Public Health at UCLA, Los Angeles, CA - Department of Radiological Science, David Geffen School of Medicine at University of California, Dept. of Biostatistics, Los Angeles, United States of America, [7]David Geffen School of Medicine at UCLA, Dept. of Hematology and Oncology, Los Angeles, United States of America, [8]Institute of Urologic Oncology (IUO), David Geffen School of Medicine at UCLA, Dept. of Hematology and Oncology, Los Angeles, United States of America

Introduction & Objectives: Thirty percent of patients with localized clear cell renal cell carcinoma (ccRCC) will ultimately develop recurrence (local or metastatic) after nephrectomy. Current risk stratification systems still misclassify patients. We have developed a novel classification integrating cytogenetic findings to better stratify the risk of recurrence and overall survival (OS) after surgery for localized ccRCC.

Materials & Methods: A total of 646 patients from UCLA with ccRCC and tumor cytogenetic analysis, were included in this study. After a selection of histologic parameters using logistic regression and cytogenetic parameters using principal component analysis a CHAID decision tree and Kaplan Meier analysis were used to build the UCLA Histo-Genetic Risk Classification (U-HGRC). Survival analyses of the model were validated on two random samples of 323 patients. Recurrence was defined as any local recurrence or development of new metastasis after surgery.

Results: The T-stage, tumor size, presence of sarcomatoid features, gain of chromosome 5q, loss 10q, or loss X/Y were used to stratify the risk of recurrence of ccRCC into three U-HGRC groups of low (1), intermediate (2) or high-risk (3). After a mean follow-up of 55 months, risk of recurrence (HR=2.44, p=.001 for U-HGRC 2; HR=9.90, p<.0001 for U-HGRC 3), disease-free survival (DFS) (Log-rank p<.0001), risk of death (HR=1.72, p=.033 for U-HGRC 2; HR=4.74, p<.0001 for U-HGRC 3) and OS (Log-rank p<.0001) were significantly different between groups. These findings were validated on two random samples. For high-risk group, median DFS and OS were 2.7 and 6.3 years, respectively. The 5-year risks of recurrence for U-HGRC group 1, 2 and 3 were 9%, 25% and 62%, respectively. The AUC of the model was significantly improved comparing to the current UISS system (0.72 for U-HGRC vs 0.65 for UISS, p=.008) with an accuracy of 82.8% for the U-HGRC high-risk group.

Figure 1: Kaplan Meier analysis of Disease-Free Survival with Greenwood 95%CI depending on U-HGRC group (Log-rank p<0.0001)



No. at risk

U-HGRC 1	291	223	185	142	114	95	79	69	57	50	44	39	33	20	14	7	5	3
U-HGRC 2	226	176	141	109	84	66	54	47	39	30	22	20	16	11	9	2	2	1
U-HGRC 3	129	75	43	34	24	17	10	8	6	6	6	5	4	1	0	0	0	0

Conclusions: The U-HGRC, which integrates genomic alterations with clinical and pathologic features, allowed a better stratification of recurrence risk and overall survival that could help to select appropriate patients for surveillance and adjuvant therapy protocols.