

Performance of a new risk assessment tool for patients with metastatic renal cell carcinoma undergoing cytoreductive nephrectomy in the targeted therapy era: REMARCC score

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Introduction & Objectives: In metastatic renal cell carcinoma (mRCC), the use of upfront cytoreductive nephrectomy (CN) has become controversial due to the outcomes of two randomized controlled trials (CARMENA/SURTIME). The objective of the current study was to examine overall survival (OS) and identify risk factors associated with patients not benefiting from CN in the targeted therapy era.

Materials & Methods: A purpose built multi-institutional international database (REgistry of MetAstatic RCC- REMARCC project) was used for this retrospective analysis. Patients with diagnosis of mRCC undergoing CN between 2004 and 2019 were included. The Kaplan Meier method and Cox proportional hazards regression analyses were used to assess overall survival (OS). Covariates statistically significant at univariable analyses were included after stepwise selection in multivariable Cox regression model. The obtained coefficients from the multivariable model were used to compute a risk score. The latter was used to predict overall mortality (OM) at 1 year. Concordance index (c-index) and decision curve analyses (DCA) were fitted to test the score as continuous variable and after stratification according to the first and second tertiles, and for comparison with standard Heng criteria.

Results: A total of 484 patients were included with a median follow-up of 48 mo (IQR:22.7-90.2). On multivariable analysis, clinical risk factors associated with decreased OS included in the final model were: Presence of sarcomatoid features (HR: 1.38, 95% CI:1.03-1.84, p=0.029), pN1 stage vs. pN0 (HR: 1.58, 95% CI:1.17-2.13, p=0.003), LDH >210 U/l (HR:1.32, 95% CI:1.04-1.68, p=0.020), calcium level >10.2 mg/dl (HR:1.98, 95% CI: 1.12-3.48, p=0.018) and bone metastases (HR:1.51, 95% CI: 1.13-2.02, p=0.005). Cox regression model showed a statistically significant correlation of the score with OM (HR:2.08, 95% CI:1.67-2.58, p<0.001). The cohort was stratified into three groups according to the score tertiles, namely low risk (23.1%), intermediate risk (40.5%) and high risk (36.4%) patients. The 1-year OS rates were 82.2 ± 3.9, 74.8 ± 3.3 and 55.1 ±

3.9% in the favorable, intermediate and low risk category, respectively. At prediction of 1-year OM, the estimated c-index for the continuous score, stratified score and Heng criteria were 61.7, 61.7 and 57.9%, respectively. DCA showed comparable performance for all the three predictors, however our score as continuous variable and after stratification showed a slightly better performance compared to the Heng's criteria when predicting 1-year OM.

Conclusions: Our analysis identifies risk factors for 1-yr OM in patients treated with CN for primary mRCC. We developed a new score based on these risk factors, which may help in personalized counselling and tailored management. The REMARCC score could be easily implemented in clinical practice.