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Introduction & Objectives: Clear cell renal cell carcinomas (CCRCC) constitute 75% of the renal cell carcinomas, have an unpredictable prognosis and show marked morphologic heterogeneity. Tumor grade and stage are the two most important independent prognostic markers. Presently, grading is done using the WHO/ISUP grading system, which is mainly nucleolar based. The recent morphologic pattern based grading system (MG) defined by Verine et al is reported to be a far better grading system for CCRCC. Thus, this study was designed to compare the prevalent ISUP/WHO and the new morphologic grading systems, their relevance to prognosis in terms of disease-free survival and overall survival, to verify whether the latter provides better predictability for the course of the disease over the former.

Materials & Methods: This was a retrospective analyses of 521 patients, ≥ 18 years, diagnosed with clear cell renal cell carcinomas (July 2014 and June 2018, follow up till Dec 2019), wherein both the above grading systems were used and compared as regards disease free survival (DFS) and overall survival (OS).

Results: Of the 521 CCRCC cases: 66.8% were males; mean age 54 years; flank pain commonest symptom; Staging 1-4: 51.8%, 8.8%, 29.6%, 9.8% respectively; WHO/ISUP grading 1-4: 39.0%, 31.5%, 13.1%, 16.5% cases respectively; Morphologic grading 1-4: 30.7%, 20.9%, 27.1%, 21.3% cases respectively. On comparing the two grading systems, WHO/ISUP Grade 1, upgraded in 71 cases, WHO/ISUP Grade 2, downgraded in 28 cases and upgraded in 73 cases, WHO/ISUP Grade 3, downgraded in 25 cases and upgraded in 16 cases and WHO/ISUP Grade 4 downgraded in 25 cases. Of the 521 patients, 291 were healthy as of December 2019, 118 recurred and 112 died due to the tumor. The mean time to recurrence was 18.61 months and that to mortality was 20.98 months. The mean overall survival was 30.12 months and mean disease-free survival was 26.93 months. Both WHO/ISUP and morphologic grading systems were statistically significant predictors for DFS and OS with $p < 0.001$. Cox PHR predicts that morphologic grading system is a more significant predictor for DFS and OS than the currently employed WHO /ISUP grading system.

Conclusions: In MG system, cases in Grade 3 & 4 are substantially high as compared to the WHO/ISUP grading. The two grading systems agreed in 54.3% cases and disagreed in 45.7% cases.

Both WHO/ISUP and MG systems are statistically significant predictors of DFS and OS, but the MG system far surpasses the former.

Lymphatic invasion, enlarged vascular spaces, sarcomatoid pattern and large nests are significant independent factors in prediction of DFS and OS. Entrapped glomeruli, rhabdoid and alveolar patterns are significant independent factors for OS. Enlarged vascular spaces upgraded a large number of WHO/ISUP Grade 1 and 2 cases to Grade 3.