

Abstract

Introduction: Chromophobe renal cell carcinoma (chRCC) is the third most common subtype of RCC after clear cell RCC and papillary RCC. It is a relatively indolent subtype of RCC with approximately 5% risk of progression and development of metastases after surgical treatment. Predicting the clinical behaviour of chRCC by histologic features has so far proven to be challenging which is related to the lack of a validated grading system for this type of renal cancer. Historically, several grading schemes were proposed specifically for chRCC. However, none of them has proven useful in clinical practice. Two main histological subtypes of chRCC are known, namely classic and eosinophilic. Moreover, several aberrant histologic subtypes have been described, including adenomatoid microcystic pigmented, multicystic, neuroendocrine, papillary, oncocytic and small cell-like. It has been previously reported that both main subtypes of chRCC (classic and eosinophilic) have no differences in their prognosis. It is hypothesized that also these rare histological subtypes are not associated with differences in clinical outcomes. Nevertheless, this hypothesis has never been tested or confirmed by clinical data.

Materials and methods: The aim of this thesis was to assess the impact of histologic diversity in chRCC (classic/eosinophilic versus rare subtypes) on survival outcome. This was realised in an international multi-institutional matched case control study including 14 institutions from 10 countries. The study group included 89 cases of rare subtypes of chRCC. The control group consisted of 70 cases of chRCC with classic and/or eosinophilic features, age- and tumor size-matched. Most of rare subtypes were adenomatoid cystic pigmented chRCC (66/89, 74,2%), followed by multicystic chRCC (10/89, 11,2%), and papillary chRCC (9/89, 10,1 %). In the control group, there were 62 (88,6%) classic and 8 (11,4%) eosinophilic chRCC.

Results: There were no statistically significant differences between the study and control group for age at diagnosis, gender distribution, tumor size, presence of tumor necrosis, presence of sarcomatoid differentiation, and adverse outcomes (disease recurrence, development of distant metastases or death due to chRCC). No statistically significant differences were found in clinical outcome between the two groups, stratified by tumor size, necrosis, and sarcomatoid differentiation.

Conclusion: The results of this work corroborated observations from previous studies that both sarcomatoid differentiation and tumor necrosis were significantly associated with poor clinical outcome in classic/eosinophilic chRCC, and this was proven to be true for chRCC with rare histologic subtypes as well. In conclusion, rare histologic patterns in chRCC without other aggressive features play no role in determining the clinical behaviour of the tumor.