



# INTROMURAL-STROMAL CELLS IN RENAL CELL CARCINOMA

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**Relevance.** Interest in studying the microenvironment of malignant neoplasms, including stromal intratumoural mast cells (MC), has remained high over the past decades. There are a small number of studies devoted to investigating the prognostic significance of MC in renal cell carcinoma (RCC). According to B. Tuna et al., the content of intratumoural TCs is significantly higher in renal cell carcinoma (RCC) than in normal renal tissue, which, according to these authors, is explained by their involvement in tumorigenesis. Thus, studies devoted to the prognostic significance of intratumoural stromal TCs in RCC are few and contradictory, and therefore this element of the tumour microenvironment needs further study. There are virtually no studies of quantitative and qualitative changes in connective tissue cells (macrophages, mast cells, neutrophils) infiltrating tumours in relation to the most important clinical and morphological factors of renal cell carcinoma (RCC) that may influence the prognosis of the disease. There are very few morphometric studies of the vascular bed of RCC, and, as is well known, computer image processing achieves very high reproducibility of results due to the large array of objects studied. Improving diagnosis and establishing objective criteria for predicting postoperative survival in patients with PC is an important issue in pathological anatomy.

**Materials and methods.** The aim of the study was to investigate intratumoural stromal TCs in PCR, to search for correlations with important clinical and anatomical factors of prognosis and postoperative survival of patients. We studied surgical material from 63 patients with CRC, of whom 34 (54%) were men and 29 (46%) were women. The average age of patients was  $58.2 \pm 1.2$  years. In all observations, CRC was classified according to the 2004 WHO classification. Based on the histological structure of the tumour, the cases were as follows: light cell carcinoma – 52 cases; papillary carcinoma – 5; chromophobe carcinoma – 3; spindle cell (sarcomatoid) carcinoma – 3. The extent of tumour spread was assessed according to the TNM classification of malignant tumours (TNM. Classification of Malignant Tumours, edited by L.H. Sobin, 2002) [1,2]. Among our patients, 47 (74.6%) corresponded to clinical stage I ( $T_1N_0M_0$ ); 3 (4.8%) corresponded to stage II ( $T_2N_0M_0$ ); stage III ( $T_1N_1M_0$ ,  $T_2N_1M_0$ ,  $T_3N_0M_0$ ,  $T_3N_1M_0$ ) – 8 (12.7%) and stage IV ( $T_4N_0M_0$ ,  $T_4N_1M_0$ ) – 5 (7.9%).

The degree of malignancy of tumour cells was assessed according to S.A. Fuhrman. G1 anaplasia corresponded to 31 (49.2%) tumours, G2 anaplasia to 14 (22.2%) tumours, G3 anaplasia to 13 (20.6%) tumours, and G4 anaplasia to 5 (8%) tumours. There were 11 (17.5%) carcinomas with regional and distant metastases and 52 (82.5%) localised tumours. The average size of the tumour node was  $7.1 \pm 0.3$  cm. Kidney tissue taken from areas as far away from the tumour as possible, without signs of inflammation or sclerosis, served as a control. The material was fixed in 10% neutral buffered formalin for 12-24 hours. Histological preparations were stained with haematoxylin and eosin and with colloidal iron according to Gale for acidic



mucopolysaccharides. TCs were detected by immunohistochemistry using monoclonal antibodies C-kit (CD117) (clone A4052, dilution 1:200, DAKO) according to the manufacturer's recommended protocol. The average number of TCs in 3 fields of view was calculated at 400x magnification.

**Results.** Analysis of TC content depending on the clinical stage of the disease according to TNM yielded the following results: in patients with stage I, the average TC count was  $1.85 \pm 0.15$ ; in stage II, the TC count increased to  $2.7 \pm 0.4$ ; in stage III, the number of TCs increased to  $4.3 \pm 0.4$ , and in stage IV, it was  $6.3 \pm 0.6$ . Thus, in stages III and IV, there was a significant increase in the number of TCs compared to stage I. When studying various histological variants of PCR, the highest average number of TCs was found in spindle cell carcinoma ( $6.3 \pm 0.6$ ), and the lowest number was found in papillary carcinoma ( $1.05 \pm 0.4$ ). Chromophobe ( $2.4 \pm 0.4$ ) and clear cell carcinoma ( $2.5 \pm 0.2$ ) occupied an intermediate position. Thus, the highest number of TCs was detected in spindle cell carcinoma, and the lowest in papillary carcinoma. In tumours of patients without regional and distant metastases, the TC content was  $2 \pm 1.2$ , and in the presence of metastases, it increased significantly to  $4.7 \pm 0.4$ .

**Conclusions.** Thus, the results of the study showed that the number of stromal TCs in a tumour is associated with a number of important prognostic clinical and anatomical factors of CRC, and therefore this parameter can be used as an additional prognostic factor. An increase in the number of TCs in a tumour can be considered a criterion for the probable occurrence of tumour metastasis.