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RESULTS OF ANALYSIS OF CLINICAL AND MORPHOLOGICAL PROGNOSIS FACTORS FOR RENAL CELL CANCER

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INTRODUCTION

In terms of incidence among malignant neoplasm, renal cell cancer (RCC) ranks tenth in the world and firmly holds the third place among malignant neoplasm of the genitourinary system.[1,2] In the structure of cancer incidence in the world population, RCC accounts for 2-3% of all malignant neoplasm, with the highest incidence in developed countries.[3] In Russia, in 2017, RCC was first diagnosed in 13556 patients. The standardized incidence rate was 16.87 per 100,000 populations, and the increase in incidence over 10 years was 42.63%. In terms of the rate of increase in the incidence of RCC, it is second only to prostate and thyroid tumors.[4] In Uzbekistan, the incidence is 2.2 per 100 thousand populations.[5] RCC is characterized by a fairly variable and unpredictable clinical course, which is due to the genetic heterogeneity and morphological diversity of this group of tumors.[6] Despite the fact that in recent years there has been an improvement in the detection of the process, more frequent detection of small tumors and early stages, the mortality rate from RCC has not undergone significant changes.[7] Therefore, the identification of factors that make it possible to make an individual prognosis and determine the optimal treatment strategy for a RCC patient is one of the most important tasks of modern oncourology.[8] Of the many prognostic parameters studied so far, the stage of the tumor when it is detected is the most predictive in relation to the probable course of the disease.[9] In the era of development of minimally invasive and ablative methods of treatment, new forms of targeted therapy and new views on the molecular mechanisms of development and progression of RCC, the identification of factors that make it possible to make an individual prognosis and determine the optimal treatment strategy for a patient with renal cell cancer is one of the most important tasks of modern oncourology.[10] Therefore, it seems relevant to conduct a study aimed at identifying the influence of various clinical and morphological parameters of renal cell cancer on survival rates.

Purpose of work: study cancer-specific survival in patients with non-metastatic renal cell cancer using clinical and morphological prognostic factors.

MATERIALS AND METHODS

This study is based on a retrospective study of data from 73 patients with renal cell cancer. Patients with localized or locally advanced renal cell cancer, depending on the size of the tumor and its location, underwent organ-preserving operations or radical nephrectomy in the period from 2014 to 2019. The characteristics of patients and tumors are shown in table 1.

Table 1: General characteristics of patients.

Total number of patients	**73**	**100%**
Men	47	64,4%
Women	26	35,6%
Age		
<40	4	5,5%
40-55	24	33%
55-70	27	37%
>70	18	24.5%
Tumor size		
<4 cm	22	30%
4-7 cm	33	45.4%

7-10 cm	12	16.4%
>10 cm	6	8.2%
T stage		
T1a	23	31.5%
T1b	20	27.5%
T2	10	13.7%
T3a	10	13.7%
T3b	5	6.8%
T4	5	6,8%
N stage		
N0	66	90.4%
N+	7	9.6%
M stage		
MO	73	100%
M1	0	0%
Histological type of tumor		
light cell c-r	65	89 %
papillary c-r	3	4.1%
chromophobic c-r	2	2.8%
sarcomatoid c-r	3	4.1%
Degree of differentiation		
G1	40	54.8%
G2	24	32.8%
G3	9	12.4%
Invasion of the tumor into the adrenal gland		
Present	2	2,7%
Invasion of the collective system		
Present	12	16.4%
Areas of tumor necrosis		
Present	26	35.6%
Multifocal tumor growth		
Present	3	4,1 %
Tumor venous thrombosis		
Present	7	9.6%

The average age of patients diagnosed with the disease is 59 years (18-84). There were 47 males (64.4%) and 26 females (35.6%). The average tumor size was 6.1 cm (1-25 cm). The most common histological types of renal cell cancer were light cell type 65 cases (89%), papillary renal cell cancer 3 cases (4.1%) and sarcomatoid renal cell cancer 3 cases (4.1%). Localized forms of renal cell cancer (stages T1 and T2) were observed in 53 cases (72.6%), while T3a, T3b and T4 stages accounted for 20 cases (27.4%). The multifocal nature of the tumor was detected in 3 (4.1%) cases. According to the degree of differentiation, the distribution of patients was as follows: high degree-40 (54.8%) cases, moderate degree - 24 (32.8%) cases, low degree - 9 (12.4%) cases. Intraoperatively, a visual increase in regional lymph nodes was detected in 11 (15%) patients, but the vast majority of patients did not have cancer metastases in regional lymph nodes. No one had distant metastases in the above group of patients. Tumor invasion into the adrenal gland was detected in 2 cases (2.7%). Areas of necrosis during histological examination of the drug were identified in 26 (35.6%) cases. Tumor thrombosis of the renal vein or inferior Vena cava occurred in 7 (9.6%) patients. Statistical processing of received data Statistical processing of data is performed using the application package "Statistica for Windows" V. 7.0, StatSoft Inc.

RESULTS AND DISCUSSIONS

The Department of urology of the Tashkent city branch Republican specialized scientific and practical medical center of Oncology and radiology, with the aim of improving the prediction of outcome in patients with renal cell carcinoma analysis of the relationship between survival rates for various clinical and morphological parameters of renal cell cancer. The parameters of the disease that directly correlated with survival were identified. Of all the studied parameters of renal cell cancer statistically significant correlation with leaders survival in the group of patients studied showed parameters such as pathologic stage of the primary tumor, tumor size, degree of differentiation, histological involvement of regional lymph nodes, tumor thrombosis of the renal or the inferior vena cava. The same parameters as the patient's gender, age, histological type of tumor, the presence of necrosis sites, and invasion of the collective system did not show a statistically

significant correlation with the survival of patients with renal cell cancer (table. 2).

Table 2: One-factor analysis of the dependence of survival on other clinical and morphological parameters of renal cell cancer.

Factor	Pearson correlation Coefficient (g), p
Gender	0,037 p=0,578
Patient's age (years)	-0,149 p=0,219
Pathological stage of the primary tumor	-0,362 p=0,002
Maximum pathological tumor size	-0,3491 p=0,003
Histological type of tumor	-0,131 p=0,281
Degree of differentiation	-0,438 p=0,001
Histological involvement of regional lymph nodes	-0,327 p=0,006
Tumor necrosis sites	-0,213 p=0,79
Renal vein thrombosis, inferior Vena cava	0,3766 p=0,03722
Invasion of the collective system	-0239 p=0,046
Tumor invasion into the adrenal gland	0,1712 p=,010

When performing a multivariate analysis of 5-year cancer-specific survival in renal cell cancer, risk ratios were determined depending on statistically significant prognostic factors. The maximum risk ratio was found between groups of tumors with a degree of differentiation of 1 and 3, the maximum size up to 4 cm and more than 4 cm in diameter (table. 3).

Table 3: Multivariate analysis of survival in renal cell cancer depending on prognostic factors.

Variables	Category	Ratio risk	Confidence interval	P
Pathological T stage	T1-2 -T3a	3,825	1,697-8,624	0,0023
	T1-2 - T3b	3,823	1,468-9,966	0,0117
Maximum pathological size	up to 4 cm- more than 4 cm	7,12	1,027-19,410	0,0096
	up to 7 cm – more than 7 cm	6,22	2,829-13,68	0,0017
	up to 10 cm – more than 10 cm	3,21	1,969 -5,247	< 0,001
Degree of differentiation	1-2	4,375	1,104-16,012	0,0355
	2-3	2,286	0,982-5,427	0,0537
	1-3	10,0	2,428-41,177	0,0355
Metastases to regional lymph nodes	N0-N+	2,857	1,5185 - 5,376	0,0477
Venous thrombosis is	present – not available	1,538	0,597-3,960	< 0,001

Single-factor and multi-factor analyses of the dependence of survival in renal cell cancer on its clinical and morphological parameters allowed us to visualize the significance of each of these parameters for predicting survival in the group of studied patients, as well as the nature of the dependence of survival rates on changes in these parameters. Traditionally, the T stage of the primary tumor is considered the most predictive in relation to the prognosis. The study of survival in groups of patients with different stages showed that the survival rate for T1a and T1b stage tumors limited by the renal capsule did not differ significantly. The five-year survival rate for the T1a stage was 93%, while for the T1b stage it was 89%. The same indicator for the T2 stage was only 50% and significantly differed from the survival rates for the T1a and T1b stages ($p<0.01$). The critical size of 7.2 cm among renal capsule-restricted tumors best separated cases of high risk of death from cases of lower risk of renal cell cancer. There was no statistically significant difference in survival rates between the stages of T3a and T3b, but in both stages, the survival rate significantly differed from the survival rate in renal capsule-restricted tumors. The risk of death from renal cell cancer is 3.8 times higher in T3a and T3b stages than in localized tumors. Stage T4 had significantly worse survival rates. No one has lived for 5 years. The 3-year survival rate was only 53%, but the prognosis was unfavorable for any size of T4 tumors. We also conducted a study aimed at identifying the critical size that can best differentiate tumors of the T3a stage into those with a relatively favorable and unfavorable prognosis. The size of 7.3 cm was also critical in the group of tumors of the T3a stage. Patients with tumors larger than 7.3 cm had a higher risk of death and those smaller than 7.3 cm had a lower risk of death compared to the risk of death identified by multivariate analysis. In

the study group of patients, we conducted a comparative analysis of the survival rates of patients with locally advanced tumors and tumors accompanied by venous tumor thrombosis, with survival rates for localized tumors of comparable sizes. The average size of the tumor in the group of localized renal cell cancer was 5.8 cm. in the group of locally common tumors the average size was 7.4 cm. Among tumors accompanied by venous tumor thrombosis, the average size was 7.2 cm. Sequential excision of small-size tumors among stages T1a, T1b, and T2 obtained groups of 23 and 10 patients, comparable in size parameters to the groups of locally advanced renal cell cancer T3a and renal cell cancer stage T3b. Neither the first nor the second comparison revealed a statistically significant difference in survival rates. In the study, the increase in tumor size, both when considered as a categorical variable and a continuous variable, was accompanied by a progressive decrease in survival rates. The results of the single-factor correlation analysis allow us to conclude that the size of the tumor can be considered as an independent prognostic factor, and its prognostic value in the likely outcome of renal cell cancer is comparable to the value of the tumor stage T. However, when predicting the likely outcome of renal cell cancer, the size of the tumor must be considered along with the stage, since tumors of identical sizes but different stages can have radically different results. However, the large size of the primary tumor, regardless of the presence or absence of local distribution, as well as the presence or absence of tumor venous thrombosis, were themselves a factor that worsens the prognosis. Tumor involvement of regional lymph nodes affected survival rates to a much more pronounced extent than local invasion or tumor sprouting of the venous system. The 3-and 5-year survival rate for regional lymph node tumors was only 52% and 26%, respectively. The risk of death from renal cell cancer at stage N+ was almost 3 times higher than at stage N0. The degree of tumor differentiation was the most strongly correlated with survival of all significant prognostic factors. There was a significant difference in survival rates in all three groups of tumors by the degree of differentiation. The risk of death from low-grade renal cell cancer was 10 times higher than for high-grade renal cell cancer.

CONCLUSIONS

The pathological stage of the tumor, the maximum pathological size, the degree of differentiation, histological involvement of regional lymph nodes, and tumor thrombosis of the renal or inferior vena cava are statistically reliable predictors of cancer-specific survival in patients with non-metastatic renal cell cancer.

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