IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 18, Issue 7 Ser. 11 (July. 2019), PP 68-73
www.iosrjournals.org

Study of Staging, Grading and Prognostic Factors of Renal Cell Carcinoma

B.H.Poorna Chandra Sekhar[1] , C.Sushma[2] , Md Khader Faheem[3] ,B.A.Ramakrishna[4], K.V.Murali Mohan[5] , B.V.Vydehi[6] ,V.Shanti[7] , N.MohanRao[8]

[1,2,3] *Assistant Professor, Department of Pathology, S.V.Medical College, Tirupati, A.P., India*
[4,6,8] *Professor, Department of Pathology, Narayana Medical College, Nellore, A.P., India*
[7] *Professor and Head, Department of Pathology, Narayana Medical College, Nellore, A.P., India*
[5] *Professor and Head, Department of Pathology, GITAM Institute of Medical Sciences and Research, Visakhapatnam, A.P., India*
**Corresponding Author: C.Sushma*

Abstract: Introduction: *Renal cell carcinoma is by far the most common malignant tumor of the kidney and it accounts for 80-85% of malignant kidney tumors. All Renal cell carcinomas are adenocarcinomas derived from renal tubular epithelial cells. The prognosis of Renal cell carcinoma depends upon age, sex, race, tumor size, histological subtype, nuclear grade, distant metastasis and pathological staging.*

Material and Methods: *The present study is both a retrospective and prospective study conducted at a tertiary care teaching hospital. Histopathological evaluation of Renal cell carcinomas was carried out for four and a half years correlating with old records, histopathology slides, special stains and immunohistochemistry. A total number of 113 nephrectomy specimens were taken into consideration in the present study. H&E stained sections of the Renal cell carcinoma specimens were studied to grade and type the tumor and to evaluate the prognostic factors. Special stains and immunohistochemistry were also used wherever required.*

Results: *A total number of 113 nephrectomy specimens were analysed and 26 diagnosed cases of Renal cell carcinoma were included in the study. Maximum number of cases were seen in 40-49 years age group (30.7%) and also in 60-69 years age group (30.7%). Maximum number of cases diagnosed were of Clear cell Renal cell carcinoma (61.5%). Least common subtype diagnosed was Collecting duct Renal cell carcinoma (3.8%). Tumor size was >4cm in maximum number of cases i.e 20 (76%). Most of the subtypes of Renal cell carcinoma had Fuhrman nuclear grades 2 and 3.*

Conclusion: *In the present study, among the histological subtypes of Renal cell carcinoma, Clear cell variant of Renal cell carcinoma was the most common histological subtype, accounting for 61.5% of cases. Nuclear grading is important in predicting survival of patients with Renal cell carcinoma. Nuclear grading is strongly related to both tumor size and stage. Nuclear grading and staging of the histological subtypes strongly influences the survival of patients, as thus proven in this study.*

Keywords: *Renal cell carcinoma, histological subtypes, tumor size, nuclear grade, pathological staging, prognosis*

Date of Submission: 15-07-2019 Date of acceptance: 30-07-2019

I. Introduction

Renal cell carcinoma is by far the most common malignant tumor of the kidney. Renal cell carcinoma accounts for 80% to 85% of malignant kidney tumors [1]. The 5-year survival rate for all stages of renal cell carcinoma improved in recent years because of an important stage migration, whereby the majority of patients are diagnosed with localized disease [2]. Many prognostic factors for survival have been identified in renal cell carcinoma, tumor stage, age, and functional status being the most significant ones [3]. Nuclear grade has also been shown to be an independent predictive factor of survival in many studies [4], higher grades correlating with the biological aggressiveness of the tumor and increased metastatic potential.

Recently, studies using current histological subtyping of renal cell carcinoma based on the American Joint Committee on Cancer and Heidelberg recommendations from 1997 or the similar WHO histological classification from 2004 have identified histology as an important prognostic factor of survival [5][6][7]. These classifications include the following distinct malignant histological subtypes: clear cell renal cell carcinoma, papillary renal cell carcinoma, chromophobe renal cell carcinoma, collecting duct renal cell carcinoma, and unclassified renal cell carcinoma.. The distinct histological subtypes have been found to have different

biological and clinical behavior affecting both the metastatic potential of the tumors and survival of the patients. Using multivariate analysis, histological subtype has been identified as an independent prognostic factor of survival in many of the studies [8]. The TNM-derived American Joint Committee on Cancer (AJCC) classification represents the gold standard staging scheme after nephrectomy for renal cell carcinoma [9].

Nuclear grade is the most important prognostic feature of a renal cell carcinoma [10][4] ; its prognostic value has been validated in numerous studies over the past eight decades. Since its definition in 1982, the Fuhrman grade represents one of the key determinants of Renal cell carcinoma-specific survival. This nuclear grading system is based on nuclear size, shape, and prominence of nucleoli [11]. The median 5-year renal cell carcinoma-specific survival is,respectively, 94%, 86%, 59%, and 31% for patients with Fuhrman grades 1, 2, 3, and 4 renal cell carcinoma [10].

The present study was designed to analyze the nephrectomy specimens , to evaluate the various prognostic factors in Renal cell carcinomas, and also to evaluate the importance of Fuhrman nuclear grading system by comparing it with other prognostic factors like tumor size, tumor stage, regional lymph node metastasis, and sarcomatoid differentiation.

II. Material And Methods

In the present study, both retrospective and prospective analysis was done in Department of Pathology, Narayana Medical College, Nellore,A.P, from January 2008 to June 2012. Diagnosis of all cases of Renal cell carcinoma was made on histopathological examination, on routine H&E stained tissue sections. In addition to H&E staining, special stains and Immunohistochemistry were done wherever necessary.

Inclusion criteria: All nephrectomy specimens with histological confirmation of Renal cell carcinoma were included in the present study.

Exclusion criteria: Non-neoplastic lesions of kidney, Benign and malignant tumors of the kidney other than Renal cell carcinoma were excluded in the present study.

Patient's history such as age, sex, laterality of nephrectomy specimens and other relevant clinical details were noted, as provided by the urologist.

III. Results

The present study was both retrospective and prospective, done during the period January 2008 to June 2012. A total number of 113 nephrectomy specimens were analysed and 26 diagnosed cases of Renal cell carcinoma were included in the study.

The age and sex distribution of Renal cell carcinomas diagnosed in the present study, are tabulated in **Table No.1** and **Table No.2** respectively. Maximum number of cases were seen in 40-49 years age group (30.7%) and also in 60-69 years age group (30.7%).

Histological subtypes of Renal cell carcinoma diagnosed were Clear cell type, Papillary type, Chromophobe type and Collecting duct type. Maximum number of cases diagnosed were of Clear cell type Renal cell carcinoma (61.5%). Least common subtype diagnosed was Collecting duct type Renal cell carcinoma (3.8%). Histological subtypes and the total number of cases diagnosed are tabulated in **Table No.3**.

Based on the tumor size, cases were categorized into three groups i.e ≤4cm, >4cm - ≤7cm and >7cm (**Table No.4**). Tumor size was >4cm in maximum number of cases i.e 20 (76%). In the present study, tumor size ranged from 2.5 cm to 14 cm, mean tumor size being 6.5 cm.

In the present study, nuclear grading of all cases of Renal cell carcinoma was interpreted using Fuhrman nuclear grading system. Grade 1 was seen in 4 cases (15.4%), Grade 2 in 10 cases (38.4%), Grade 3 in 11 cases (42.3%), and Grade 4 in one case (3.8%). Most of the Renal cell carcinomas had grades 2 and 3. Subtypes of Renal cell carcinoma and their corresponding nuclear grades is tabulated in **Table No.5**.

Out of 26 cases of Renal cell carcinoma, sarcomatoid differentiation was observed histologically in 3 cases (11.54%) within the tumor tissue. 2 cases of Clear cell type and 1 case of papillary type of Renal cell carcinoma had sarcomatoid differentiation (**Table No.6**).

AJCC-TNM staging scheme (2002) was applied to all the cases of Renal cell carcinoma. Number of cases and their corresponding Primary tumor stage (pT), status of Regional lymph node metastasis (N), and assessment of Distant metastasis was done and the observations are tabulated in **Table No.7**, **Table No.8** and **Table No.**9 respectively.

TABLE No.1. Age distribution

AGE GROUP	Clear cell	Papillary	Chromophobe	Collecting duct	TOTAL	PERCENTAGE (%)
< 40	1	0	1	0	**2**	7.70
40-49	5	3	0	0	**8**	30.77
50-59	5	1	1	0	**7**	26.92
60-69	4	2	1	1	**8**	30.77
70-79	1	0	0	0	**1**	3.84

≥ 80	0	0	0	0	**0**	0.00
TOTAL	**16**	**6**	**3**	**1**	**26**	**100**

TABLE No.2. Sex distribution

SEX	Clear cell	Papillary	Chromophobe	Collecting duct	TOTAL	PERCENTAGE (%)
MALE	11	4	2	1	18	69.23
FEMALE	5	2	1	0	8	30.77
TOTAL	16	6	3	1	26	**100**
M:F	2.2:1	2:1	2:1		**2.2:1**	

TABLE No.3. Histological subtypes of Renal cell carcinoma

HISTOLOGICAL SUBTYPE	NO. OF CASES	TUMOR SIZE RANGE
Clear cell renal cell carcinoma	16	2.5-12 cm
Papillary renal cell carcinoma	6	5-8 cm
Chromophobe renal cell carcinoma	3	3.5-14 cm
Collecting duct renal cell carcinoma	1	9 cm
TOTAL	**26**	

TABLE No.4. Tumor size

TUMOR SIZE	NO. OF CASES	PERCENTAGE (%)
≤ 4 cm	06	23.08
> 4cm - ≤ 7 cm	10	38.46
> 7 cm	10	38.46
TOTAL	**26**	**100**

TABLE No.5. Fuhrman nuclear grading

SUBTYPE of Renal cell carcinoma	GRADE 1	GRADE 2	GRADE 3	GRADE 4	TOTAL
Clear cell	3	6	6	1	**16**
Papillary	0	2	4	0	**6**
Chromophobe	1	1	1	0	**3**
Collecting duct	0	1	0	0	**1**
TOTAL	**4**	**10**	**11**	**1**	**26**
PERCENTAGE (%)	**15.39**	**38.47**	**42.30**	**3.84**	**100**

TABLE No.6. Sarcomatoid differentiation

Sarcomatoid differentiation	Clear cell	Papillary	Chromophobe	Collecting duct	TOTAL	Percentage (%)
PRESENT	2	1	0	0	3	11.54
ABSENT	14	5	3	1	23	88.46
TOTAL	**16**	**6**	**3**	**1**	**26**	**100**

TABLE No.7. Primary tumor stage (pT)

PRIMARY TUMOR (pT)	NO. OF CASES	PERCENTAGE (%)
T1	14	53.84
T2	6	23.08
T3	6	23.08
T4	0	0
TOTAL	**26**	**100**

TABLE No.8. Regional Lymph node metastasis (N)

PRIMARY TUMOR (pT)	NO. OF CASES	PERCENTAGE (%)
T1	14	53.84
T2	6	23.08
T3	6	23.08
T4	0	0
TOTAL	**26**	**100**

TABLE No.9. Distant metastasis

DISTANT METASTASIS (M)	NO. OF CASES	PERCENTAGE (%)
MX	26	100
M0	0	0
M1	0	0
TOTAL	**26**	**100**

IV. Discussion

A total number of 113 nephrectomy specimens were analysed and 26 diagnosed cases of Renal cell carcinoma were included in the present study. The retrospective and prospective study with regards to Renal cell carcinoma was done in a detailed manner. Renal cell carcinoma is by far the most common malignant tumor of the kidney, accounting for 3% of adult malignancies.

The incidence of renal cell carcinoma increases with age, with a peak in the sixth decade of life and a median patient age of 55 years. Renal cell carcinoma in our study occurred in a wide age range from 30 years to 70 years. Renal cell carcinoma was not seen among children in our study. Right kidney was most commonly involved than the left one. In present study the highest number of cases with renal cell carcinoma was observed in the 4^{th} and 6^{th} decades of life **(Table No.10)**, which was similar to the studies done by Leclercq et al [12] and T. Gudbjartsson et al [13], majority of the cases were in the 6^{th} decade.

According to the literature men are more often affected than women in a ratio approximately 1.5 to 1. In the present study, males were most commonly affected than females with incidence of 69.2%, and male to female ratio of 2.2:1 which was similar to studies done by Leclercq et al [12] and Karakiewicz et al [14], **(Table No.11)**.

To date, several prognostic indicators including tumor stage, tumor size, Furhman nuclear grade, and symptom classification have been shown to predict renal cell carcinoma-specific survival after nephrectomy [15]. The maximum size of a renal cell carcinoma that correlates with behavior and should determine stage has been surprisingly controversial over the years. A greatest dimension of 4 cm seems to provide the most acceptable cut-off point [16]. In the present study the mean tumor size was 6.5 cm which was strongly correlating with the study done by Leclercq et al [12] and was similar to the study done by Karakiewicz et al [14] **(Table No.12).**

Recently, studies using current histological subtyping of renal cell carcinoma based on the UICC/AJCC and Heidelberg recommendations from 1997[17] or the similar WHO histological classification from 2004[18] have identified histology as an important prognostic factor of survival [5]. In the present study clear cell renal cell carcinoma was the most common histological subtype (61.54 %) followed by papillary variant (23.07%), chromophobe renal cell carcinoma (11.54%), and collecting duct renal cell carcinoma (3.85%). The study was comparable with the study done by Rainwater et al and R. Houston et al [19], in their study they also documented clear cell renal cell carcinoma as a predominant variant followed by papillary renal cell carcinoma. One case (3.85%) of collecting duct renal cell carcinoma was documented in the present study **(Table No.13)**. The distinct histological subtypes have been found to have different biological and clinical behaviour affecting both the metastatic potential of the tumors and survival of the patients. Histological subtype has been identified as an independent prognostic factor of survival in many of the studies.

With the exception of stage, nuclear grade is the most important prognostic factor of a renal cell carcinoma [10]; its prognostic value has been validated in numerous studies over the past eight decades. The Fuhrman nuclear grading system is an established predictor of survival in patients with renal cell carcinoma. Grade is also strongly related to both tumor size and the pathologic staging, higher grades implying increased metastatic potential of the primary tumor and biological aggressiveness with reduced survival as a result. This nuclear grading system is based on nuclear size, shape, and prominence of nucleoli [11]. In the present study 4 cases (15.4%) had grade 1, 10 cases had grade 2 (38.5%), 11 cases had grade 3 (42.3%), and one case had grade 4 (3.8%). Maximum number of cases were having grades 2 and 3 (21 cases; 80.8%).The present study was similar to studies done by T. Gudbjartsson et al [13] and Leclercq et al [12]. In the study done by T. Gudbjartsson et al [13], 50.1% (313) of cases had grade 2 nuclear features and 35.8% (224) of cases had grade 3. In the study conducted by Leclercq et al [12], 42% (2289) of cases had grade 2 and 29.4% (1602) of cases had grade 3 features **(Table 14)**.

Sarcomatoid renal cell carcinoma is not a distinct histologic entity and represents high-grade transformation in different subtypes of renal cell carcinoma. The presence of a sarcomatoid component in a renal cell carcinoma is widely considered to be a poor prognostic sign and has sufficient patient care implications to warrant inclusion in the diagnosis. The amount of sarcomatoid histology required for diagnosis has not been defined but the suggestion that the sarcomatoid area comprise at least one low-power (4X) field seems reasonable [20]. There is controversy as to whether the amount of sarcomatoid tumor is relevant when analyzing the disease's potential for recurrence. In our study, 3 cases (11.54%) of renal cell carcinoma showed a sarcomatoid component within the tumor tissue, out of which two were in clear cell renal cell carcinoma cases and one in papillary renal cell carcinoma case. Tumors which showed sarcomatoid differentiation in our study had higher nuclear grades i.e Grade 2 and Grade 3 and this observation was correlating with the study done by de Peralta – Venturina et al [20]. Sarcomatoid change in renal cell carcinoma protends a worse prognosis.

The prognosis of patients with renal cell carcinoma is influenced by multiple factors, including nuclear grade, tumor size, infiltrative margin, tumor stage, and histologic type, but tumor stage is the most important determinant of outcome [21]. The TNM staging system of the AJCC is recommended. In the present study the

most common primary tumor staging was T1 accounting for 53.84% (14 cases). This correlates with the studies conducted by Leclercq et al [12] and Karakiewicz et al [14]. It is well known that nodal involvement is one of the major factors influencing the prognosis of cancer patients, including patients with renal cell carcinoma. In our study, 11.5% (3) of the cases had regional nodal metastasis which was a little bit higher when compared to other studies conducted by Leclercq et al [12] and T. Gudbjartsson et al [13] **(Table 15)**. This slight variation in the present study may be due to a small study group.

TABLE No.10. Age distribution in various studies

DIFFERENT STUDIES	**COMMON AGE GROUP**	**MEAN AGE**
Leclercq et al. (2007)	6th decade	60.5 years
Karakiewicz et al. (2007)	6th decade	60.7 years
T. Gudbjartsson et al. (2005)	6th decade	64.0 years
Present study (2012)	**4th & 6th decades**	**42.4 years**

TABLE No.11. Sex distribution in various studies

	Leclercq et al. (2007) N=5453	Karakiewicz et al. (2007) N=2530	T. Gudbjartsson et al. (2005) N=629	**Present study N=26**
MALES	67.7%	66.6%	61.7%	**69.2%**
FEMALES	32.3%	33.4%	38.3%	**30.8%**
M:F RATIO	2.1:1	2:1	1.6:1	**2.2:1**

TABLE No.12. Mean tumor size in various studies

	Leclercq et al. (2007 N=5453	Karakiewicz et al. (2007) N=2530	T. Gudbjartsson et al. (2005) N=629	**Present study (2012) N=26**
MEAN TUMOR SIZE (Cm)	6.4	6.7	7.4	6.5

TABLE No.13. Histological subtypes documented and their incidence in various studies

	Rainwater et al (1986) N:41	Soroush Rais et al (2008) N:32	R.Houston et al (2009) N:2691	**Present study N:26**
HISTOLOGICAL SUBTYPES				
Clear cell	82%	75.8%	62.5%	**61.54%**
Papillary	12%	9.9%	12.59%	**23.07%**
Chromophobe	-	12.1%	9.0%	**11.54%**
Collecting duct	-	1.1%	0.22%	**3.85%**

TABLE No.14. Fuhrman nuclear grades in various studies

NUCLEAR GRADE	Leclercq et al. (2007) N=5453	Karakiewicz et al. (2007) N=2530	T. Gudbjartsson et al. (2005) N=629	**Present study N=26**
GRADE 1	21.2% (1156)	26.3% (665)	3.8% (24)	**15.4% (4)**
GRADE 2	42% (2289)	33.0% (835)	50.1% (313)	**38.5% (10)**
GRADE 3	29.4% (1602)	32.9% (832)	35.8% (224)	**42.3% (11)**
GRADE 4	7.4% (406)	7.8% (198)	10.3% (64)	**3.8% (1)**

TABLE No.15. TNM Staging in various studies

	Leclercq et al. (2007) N=5453	Karakiewicz et al. (2007) N=2530	T. Gudbjartsson et al. (2005) N=629	**Present study N=26**
PRIMARY TUMOR (T)				
T1	49.4% (2694)	46.9% (1187)	29.9% (188)	**53.84% (14)**
T2	13.9% (759)	15.3% (387)	13.5% (85)	**23.08% (6)**
T3	35.1% (1912)	35.6% (900)	24.3% (153)	**23.08% (6)**
T4	1.6% (88)	2.2% (56)	32.3% (203)	**0% (0)**
REGIONAL				

METASTASIS (N)				
N (+)	7.8% (424)	9.1% (231)	9.6% (61)	**11.5% (3)**
DISTANT METASTASIS (M)				
M (+)	12.5% (684)	12.8% (327)	12.8% (81)	**0% (0)**

V. Conclusion

The current study underscores the importance of nuclear grading in predicting survival of renal cell carcinoma patients. There is strong correlation between grade, tumor size, and stage. Different histological subtypes confer different survival, but in spite of the distinctive cytogenetic and molecular characteristics of the tumors, the survival difference is to a large extent due to differences in stage and grade, histological type not being an independent prognostic factor of survival in multivariate analysis. Sarcomatoid change in renal cell carcinoma protends a worse prognosis. Because tumors with even a small component of sarcomatoid change may have an adverse outcome, this finding when present, should be noted in the surgical pathology report. Tumor size is not an independent predictor for the histological subtype of renal cell carcinoma. However, it is closely correlated to histopathological features, with the indications that the greater the tumor size, the more aggressive potential the renal cell carcinoma is. Nodal involvement is one of the major factors influencing the prognosis of cancer patients, including patients with renal cell carcinoma. Involvement of lymph nodes is correlated with advanced T stage and concomitant distant metastases. Lymph node dissection definitely improves staging and does not add to the morbidity of radical nephrectomy. Stage and grade, together with age and calendar year of diagnosis, are therefore the most important prognostic factors of survival for patients with renal cell carcinoma.

References

[1]. Cohen HT, McGovern FJ. Renal-cell carcinoma. N Engl J Med. 2005; 353: 2477– 2490.
[2]. Pantuck AJ, Zisman A, Belldegrun AS. The changing natural history of renal cell carcinoma. J Urol. 2001; 166: 1611–1623.
[3]. Ficarra V, Righetti R, Pilloni S, et al. Prognostic factors in patients with renal cell carcinoma: retrospective analysis of 675 cases. Eur Urol 2002; 41(2): 190–8.
[4]. Lohse CM, Blute ML, Zincke H, Weaver AL, Cheville JC. Comparison of standardized and nonstandardized nuclear grade of renal cell carcinoma to predict outcome among 2,042 patients. Am J Clin Pathol 2002; 118: 877-86.
[5]. Kovacs G, Akhtar M, Beckwith BJ, et al. The Heidelberg classification of renal cell tumors. J Pathol 1997; 183(2): 131-3.
[6]. Eble JN, Sauter G, Epstein JI, Sesterhenn IA, eds. World Health Organization classification of tumors: pathology and genetics of tumours of the urinary system and male genital organs. Lyons: IARC Press; 2004.
[7]. Lau WK, Cheville JC, Blute ML, Weaver AL, Zincke H. Prognostic features of pathologic stage T1 renal cell carcinoma after radical nephrectomy. Urology 2002; 59(4): 532–7.
[8]. Beck SD, Patel MI, Snyder ME, et al. Effect of papillary and chromophobe cell type on disease-free survival after nephrectomy for renal cell carcinoma. Ann Surg Oncol 2004; 11(1): 71–7.
[9]. Gettman MT, Blute ML, Spotts B, Bryant SC, Zincke H. Pathologic staging of renal cell carcinoma: significance of tumor classification with the 1997 TNM staging system. Cancer 2001; 91: 354-61.
[10]. Ficarra V, Righetti R, Martignoni G, et al. Prognostic value of renal cell carcinoma nuclear grading: multivariate analysis of 333 cases. Urol Int 2001; 67: 130-4.
[11]. Fuhrman SA, Lasky LC, Limas C. Prognostic significance of morphologic parameters in renal cell carcinoma. Am J Surg Pathol 1982; 6: 655-63.
[12]. Nathalie Rioux-Leclercq, Pierre I. Karakiewicz, Quoc-Dien Trinh, Vincenzo Ficarra, Luca Cindolo, Alexandre de la Taille et al. American Cancer Society 2007; 109: 868-874.
[13]. Tomas Gudbjartsson, Sverrir Hardarson, Vigdis Petursdottir, Asgeir Thoroddsen, Jonas Magnusson, Gudmundur V. Einarsson. Histological Subtyping and Nuclear Grading of Renal Cell Carcinoma and Their Implications for Survival: A Retrospective Nation-Wide Study of 629 Patients. Eur Urol 2005; 48: 593-600.
[14]. Pierre I. Karakiewicz, Alberto Briganti, Felix K.-H. Chun, Quoc-Dien Trinh, Paul Perrotte, Vincenzo Ficarra et al. Multi-Institutional Validation of a New Renal Cancer–Specific Survival Nomogram. J Clinical Oncol 2007; 25: 1316-1322.
[15]. Ficarra V, Guille F, Schips L, et al. Proposal for revision of the TNM classification system for renal cell carcinoma. Cancer. 2005; 104: 2116-2123.
[16]. Gettman MT, Blute ML. Update on pathologic staging of renal cell carcinoma. Urology 2002; 60: 209-17.
[17]. Kovacs G, Akhtar M, Beckwith BJ, et al. The Heidelberg classification of renal cell tumors. J Pathol 1997; 183(2): 131-3.
[18]. Eble JN, Sauter G, Epstein JI, Sesterhenn IA, eds. World Health Organization classification of tumors: pathology and genetics
[19]. of tumours of the urinary system and male genital organs. Lyons: IARC Press; 2004.
[20]. R. Houston Thompson, Jordon, Matthew, Satish. K. Tumor size is associated with malignant potential in renal cell carcinoma cases. Journal of Urology. 2009; 181: 2033-36.
[21]. de Peralta-Venturina M, Moch H, Amin M, et al. Sarcomatoid differentiation in renal cell carcinoma: a study of 101 cases. Am Surg Pathol 2001; 25: 275-84.
[22]. Gelb AB. Renal cell carcinoma: current prognostic factors. Union Internationale Contre le Cancer (UICC) and the American Joint Committee on Cancer (AJCC). Cancer 1997; 80: 981-6.