

# Renal cell carcinoma – correlation of fuhrman grading with prognostic factors

Hassan Sona Rai<sup>1\*</sup>, Shilpa Premkumar<sup>2</sup>, Prema Saldanha<sup>3</sup>

<sup>1,2</sup>Resident, <sup>3</sup>Professor, Department of Pathology, Yenepoya Medical College, Deralakatte, Mangalore-575018, Karnataka, INDIA.

Email: [sonarai99@gmail.com](mailto:sonarai99@gmail.com)

## Abstract

Renal tumors are the third most frequent genitourinary tract tumors, accounting for 2-6% of all malignancies. Renal cell carcinoma (RCC), clear cell type is the most common variant of renal epithelial tumors, accounting for 2% of all malignancies and about 70% of RCCs. It occurs primarily in adult seen in age group of sixth to seventh decades. Renal cell carcinoma, clear cell type has a male predominance of 2:1. Haematuria is the single most common presenting sign. Less than 10% of the cases present with classic triad of flank mass and pain. Fuhrman nuclear grade is considered to be independent prognostic factor in renal cell carcinomas which determines the patient outcome. This study is done to analyse the clear cell carcinomas with respect to their Fuhrman nuclear grade and morphological prognostic factors.

**Keywords:** Renal cell carcinoma, Fuhrman grade, prognosis.

## \*Address for Correspondence:

Dr. Hassan Sona Rai, Resident, Department of Pathology, Yenepoya Medical College, Deralakatte, Mangalore-575018, Karnataka, INDIA.

Email: [sonarai99@gmail.com](mailto:sonarai99@gmail.com)

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## INTRODUCTION

Renal cell carcinoma (RCC) is generally a tumor of adults with average age being 55-60 years. Many of the renal cell carcinomas occurring in children have behavior equivalent to those of adults. RCC is the most common type of kidney cancer. Nephrectomy remains the treatment of choice and therapeutic modality for the patients to free them of pain and varied chronic life debilitating and destructive conditions. Various systems have been used for the grading of renal cell carcinoma (RCC). This Fuhrman grading system used here is based on classification of RCC into four categories according to nuclear size and the presence of nucleoli, which is widely used in North America and Europe.<sup>1</sup> Radical nephrectomy till date is the only promising treatment which significantly increases survival in patients with organ confined disease.<sup>2</sup> Clear cell renal cell carcinoma (ccRCC) forms the majority with 70% diagnosed by light

microscopy as ccRCC. Clear cell renal carcinoma originates from the proximal tubule and grossly can appear cystic or solid.<sup>3</sup> Fuhrman (1982), introduced a histological classification with prognostic value in ccRCC with further years has become necessary for management and prognosis of the renal tumor, especially ccRCC.<sup>4</sup> This study analyzes the clear cell carcinoma of the kidney according to the age, gender, site, histopathology and Fuhrman grades.

## MATERIALS AND METHODS

This study was done retrospectively on fourteen nephrectomy specimens. Grossing was done according to standard protocol.<sup>5</sup> formalin-fixed tissues were processed by the routine procedure and paraffin embedded. Sections of 4-5 microns thickness were cut and stained with hematoxylin and eosin. These sections were analyzed in detail by light microscopy.

### Inclusion Criteria

In our study specifically selected clear cell renal carcinoma from various other types of renal cell carcinoma reported in the department.

### Exclusion Criteria

In our study were histopathologically confirmed benign lesions, other variants of renal cell carcinoma and other malignant lesions such as transitional cell carcinoma and lymphomas. The nuclear grading was done according to the Fuhrman grading system. According to this, the Nuclear grading for ccRCC is as follows:

G1: Small, round, uniform with absent or inconspicuous nucleoli;  
 G2: Larger nuclei with irregular contour and nuclei visible at x400;  
 G3: Still larger nuclei with obviously irregular contours and large nucleoli;  
 G4: Nuclei generally similar to G3 with bizarre, contours and chromatin clumps.<sup>6</sup>

**OBSERVATION AND RESULTS**

The present study was carried out on a total of fourteen nephrectomy specimens. The most common age group involved in clear cell renal cell carcinoma between 70 to 79 years constituting 42.9% of all the tumors studied followed by four cases in the age group of 50 -59 years. We had three cases from the age group 60 – 69 years and one case in age group 20 – 29. The male: female

comparison, males are commonly involved in clear cell renal cell carcinoma being 92.6%. In the 14 cases studied it showed that 50 % of the cases had symptoms of flank pain. The majority of the tumors were between the size 3 – 12 cms. Necrosis and hemorrhage were present in all 14 cases studied. Renal vein involvement was seen in 4 cases studied and perinephric fat infiltration was seen in 3 cases studied. 42.9% of the cases were grade I (Figure 1), 35.7% were Grade II (Figure 2) and 21.4% were Grade III (Figure3). There were no cases in grade 4 recorded. Table 1 shows the correlation between Fuhrman grade, tumor size, presence of necrosis or hemorrhage, renal vein invasion, renal pelvis involvement and stage of the tumor. A correlation between grade and stage was found with the cases which were grade I were in stage I. There was no correlation seen in with tumor size, and the presence of necrosis and hemorrhage.

**Table 1:** Showing the grade, tumor size, necrosis or hemorrhage, renal vein invasion, renal pelvis involvement and stage of the tumor.

Fuhrman Grade	Tumour size	Necrosis / hemorrhage	Renal vein involvement	Renal pelvis involvement	Stage
I	<3 -	-	-	-	-
	3-12 - 6	Necrosis -6 hemorrhage-6	1	0	Stage I – 4 Stage II - 1 Stage III - 1 Stage IV - 0
II	>12 - <3 -	- -	- -	- -	- -
	3-12 - 4	Necrosis-4 hemorrhage - 4	2	1	Stage I – 3 Stage II - 0 Stage III - 1 Stage IV – 0
III	>12 - <3 -	- -	- -	- -	- -
	3-12 - 4	Necrosis-4 hemorrhage - 4	1	2	Stage I – 0 Stage II - 0 Stage III - 4 Stage IV – 0
IV	>12 - -	- -	- -	- -	- -

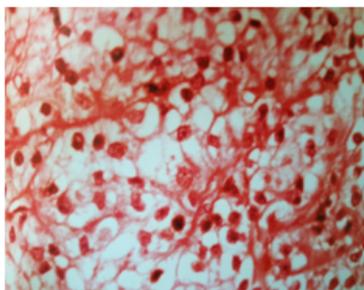


Figure 1

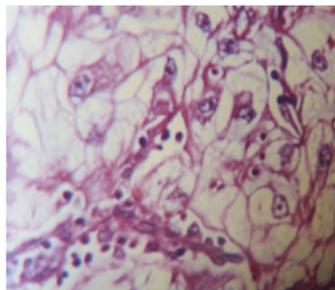


Figure 2

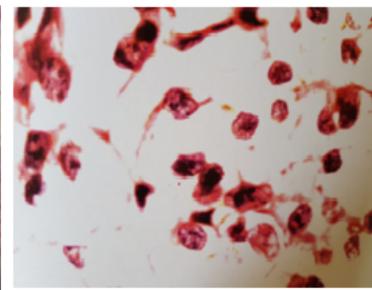


Figure 3

**Legend**

Figure 1: Microphotograph of Clear cell renal carcinoma with Fuhrman nuclear grade I (H and E, 40X)

Figure 2: Microphotograph of Clear cell carcinoma with Fuhrman nuclear grade II(H and E, 40 X)

Figure 3: Microphotograph of Clear cell renal cell carcinoma of nuclear grade III (H and E, 40X)

## DISCUSSION

Renal cell carcinoma is the third most frequent urological malignancy after prostate carcinoma and bladder carcinoma ccRCC form 90% of renal cell carcinoma.<sup>7</sup> The 4 point multiparametric scale of Fuhrman grading is based on size, shape, chromasia and nucleolar prominence.<sup>8</sup> Fuhrman classification system of nuclear grading is widely accepted and has been shown to confer prognostic significance.<sup>9</sup> Urologists in North America and Europe use Fuhrman nuclear grading system commonly.<sup>10</sup> In 1982, Fuhrman *et al* performed the nuclear grading on the microscopic morphological features of clear cells in clear cell renal cell carcinomas using hematoxylin and eosin stained sections.<sup>11</sup> Clear cell renal cell carcinoma comprise two thirds to three quarters of all renal cell carcinoma. This name is given to these tumors because most of them are composed mainly or partially of cells with abundant clear cytoplasm. Clear cell renal cell carcinoma are characterized by loss of genetic material on 3p. The loss ranges from loss of the whole chromosome to loss of function through hypermethylation. Alteration on chromosome 14, 8 and 9 affect prognosis, with a worse outcome in several studies. Clear cell renal cell carcinomas arise from renal cortex, go inward and are diffusely infiltrative. Cut surface shows a solid, golden – yellow brown tumor. Hemorrhage, necrosis, calcification and cystic change result in variegated appearance. ccRCC invades renal vein and 5% have sarcomatoid change. Microscopically the prominent delicate vasculature surrounding alveolar clusters of cells is typical of clear cell renal cell carcinoma. Also seen are solid sheets of alveoli. The tumor cells of clear cell carcinoma are large and the cytoplasm ranging from optically clear, with sharply outlined boundaries. The clear cell appearance of the tumor cells results from the accumulation of glycogen and fat. The tubules and small cysts filled with eosinophilic proteinaceous fluid or fresh hemorrhage are typical of clear cell renal cell carcinoma. Psammoma bodies and foamy macrophages are rarely to be seen in ccRCC.<sup>12</sup> Clear cell renal cell carcinoma has worst prognosis compared to the other common types of renal cell carcinomas. However, clear cell renal cell carcinoma is merely a name, and many of these carcinomas have extensive areas in which the cytoplasm is eosinophilic.

The overall 5 year survival rate for renal cell carcinoma is approximately 70%. The prognosis of patients discussed here depends on staging, tumor size, renal vein invasion and microscopic grade. There are 4 stages: Stage I confined to the kidney; Stage II – extension to perirenal fat but within Gerota's fascia; Stage III – renal vein or vena caval involvement or regional lymph nodes

metastasis and Stage IV – extension to adjacent organs other than adrenal or distant metastases.

Fuhrman nuclear grade of the tumor as determined in microscopic sections is an important predictor of survival. It is correlated with surgical staging. There are four nuclear grades. Grade I and grade II have better prognosis than compared to grade III and grade IV. The size of primary tumor assists in the prognosis of the patient. It is divided into <3cm, 3 -12 cms and > 12 cms. A tumor size of or less than 5 or 5.5cm is considered with a better survival rate after nephrectomy. In the study done by Medeiros *et al*, grading done by nuclear criteria was reported to be significant prognostic factor when compared to the greatest tumor dimension.<sup>13</sup> In our study there was no correlation with tumor size. Renal vein invasion is a poor prognostic therefore presence of renal vein invasion affects the outcome of the patient. Rey *et al* evaluated whether tumor necrosis, microvascular invasion, and invasion of the renal sinus could appear as independent prognostic factors. It was evident that these new variables were associated with cancer-specific survival, although they were not independent prognostic factors.<sup>14</sup> Studies done by Bretheau *et al* showed 5 year survival rates of the patients with grade I,II,III and IV tumors was 76%, 72%,51%, and 35%, respectively.<sup>15</sup> An American study was done by Sun *et al*<sup>16</sup> in which only patients with clear cell renal cell carcinoma, which concluded that the use of two or three groups maintains the prognostic value as heterogeneity is seen in grade III and grade IV. Fuhrman grade IV often have factors that cloud the overall perception such as greater tumor size, higher degree of necrosis, or increased microvascular involvement and sarcomatoid differentiation.

## CONCLUSION

Fuhrman nuclear grading is considered to be an independent prognostic factor in renal cell carcinoma which determines the patient outcome. This study shows that grade I tumors are associated with a lower stage while the stage is higher in a tumor with a higher grade.

## REFERENCES

1. Fuhrman S, Lasky LC, Limas L. Prognostic significance of morphologic parameters in renal cell carcinoma. *Am J Surg Pathol.* 1982; 6:655-663.
2. Robson CJ, Churchill BM, Anderson W. Results of radical nephrectomy for renal cell carcinoma. *J Urol* 1969; 101:297-301.
3. Presti JC jr, Rao PH, Chen Q, et al. Histopathological, cytogenetic, and molecular characterization of renal cortical tumors. *Cancer Res* 1991; 51:1544.
4. Moran E, Rogel R, Soto A, Ruiz C, Budia A, Salom JV, Jimenez Cruz JF. Usefulness of new schemes

- to group Fuhrman grades in clinical practice for clear cell renal tumor. *Actas urol esp.* 2012; 36:352-8.
5. Zisman A, Pantuck A, Wiedner J, et al. Risk group assessment and clinical outcome algorithm to predict the natural history of patients with surgically resected renal cell carcinoma. *J clin oncol.* 2002; 20:4559-66.
  6. Ficarra V, Martignoni G, Maffei N. Original and reviewed nuclear grading according to the Fuhrman system. *American cancer society.* 2004; 103:68-75.
  7. Merjean A, Oudard S, Thionn N. Prognostic factors of renal cell carcinoma. *J urol.* 2003; 169:821-7.
  8. Lawrence D, True MD. The time for accurate Fuhrman grading of renal cell carcinomas has arrived. *Am j Clon Pathol* 2002; 118:827-9.
  9. Hsu R. M, Chan DY, Siegelman SS. small renal cell carcinoma: correlation of size with tumor stage, nuclear grade, and histologic subtype. *Ajr.* 2004; 182:551-7.
  10. Leibovich BC, Pantuck AJ, Bui MH, et al. Current staging of renal cell carcinoma. *Urol Clin North Am.* 2003; 30:481-97.
  11. Sun M, Lughezzani G, Jeldress C, et al. A proposal for reclassification of the fuhrman grading system in patients with clear renal cell carcinoma. *Eur urol* 2009; 52(5):775-81.
  12. Medeiros LJ, Jones EC, Aizawa S, et al. Grading of renal cell carcinoma. Workshop no.2. *Cancer* 1997; 80:990-91.
  13. Rosai J, Order N. Urinary tract. In ackerman's surgical pathology. 10<sup>th</sup> edition. St louis missouri: mosby2004:1237-342.
  14. Rioux- Leclercq Taille A, et al. Prognostic ability of simplified nuclear grading of renal cell carcinoma. *Cancer.* 2007; 109:868-74.
  15. Bretheau D, Lechevallier E, de Fromont M, Sault MC, Rampal M and Coulange c. Prognostic value of nuclear grade of renal cell carcinoma. *cancer.* 1995.15;76(12):2543-9.
  16. Sun M, Lughezzani G, Jeldres C, Isbarn H, Shariat SF, Arjane P. A proposal for reclassification of the Fuhrman grading system in patients with clear renal cell carcinoma. *Eur urol.* 2009; 56:775-81.

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