

# PREDICTIVE FACTOR OF METASTATIC RENAL CELL CARCINOMA PATIENT IN SARDJITO HOSPITAL PERIOD 2010 - 2015

**<sup>1</sup>Moch. Abdul Kohar, <sup>1</sup>Untung Tranggono.**

<sup>1</sup>Division of Urology/Department of surgery, Faculty of Medicine/Gadjah Mada University, Sardjito General Hospital, Yogyakarta.

## ABSTRACT

**Objective:** To analyze the association between various prognostic factors and the incidence of renal cell carcinoma (RCC) metastatic. **Material & methods:** This is a descriptive retrospective study. In this research, the dependent variable is metastatic RCC while the predictor factor as independent variable influencing renal cell carcinoma metastasis. The study population were all patients with renal cell carcinoma that were diagnose in Sardjito Hospital from period 2010 to 2015. **Results:** In this study there were 34 patients who became the object of research. Consisting of men as many as 20 people (58.8%) while women as many as 14 people (41.2%), while for the age category <51 years as many as 16 people (47.1%) while RCC patients aged > 51 years old 18 People (52.9%). In this study, patients with RCC mostly found in stage 2 were 15 people (44.1%), stage 3 of 6 people (17.6%), stage 4 were 13 people (38.2%). These results are consistent with previous studies which suggest that RCC is found most frequently in stage 2 (Soblin et al, 1997). The p value = < 0.038 indicates that there is a significant correlation between tumor staging and metastatic occurrence in RCC, the result of this study is similar to the previous study which stated that the higher the staging of the tumor the greater the risk of metastasis with p value = 0.001 (Vina et al., 2016). **Conclusion:** There was a significant association between staging of renal cancer and metastatic events.

**Keywords:** Renal cell carcinoma, metastatic predictive factor.

## ABSTRAK

**Tujuan:** Menganalisa hubungan antara bermacam faktor prognostik dan kejadian metastasis renal cell carcinoma (RCC). **Bahan & cara:** Penelitian ini merupakan penelitian retrospektif deskriptif. Pada penelitian ini variabel terikat berupa metastasis renal cell carcinoma sedangkan faktor prediktor sebagai variabel bebas yang berpengaruh terhadap metastasis renal cell carcinoma. Populasi penelitian adalah seluruh pasien dengan diagnosis renal cell carcinoma di RSUP Dr. Sardjito periode tahun 2010 sampai dengan tahun 2015. **Hasil:** Pada penelitian ini terdapat 34 pasien yang menjadi obyek penelitian, terdiri dari laki-laki sebanyak 20 orang (58.8%) sedangkan perempuan sebanyak 14 orang (41.2%), sedangkan untuk kategori usia <51 tahun sebanyak 16 orang (47.1%) sedangkan pasien RCC dengan usia >51 tahun sebanyak 18 orang (52.9%). Pada penelitian ini, pasien dengan RCC paling banyak temukan pada stadium 2 yaitu sebanyak 15 orang (44.1%), stadium 3 sebanyak 6 orang (17.6%), stadium 4 sebanyak 13 orang (38.2%). Hasil tersebut sesuai dengan studi sebelumnya yang menyatakan RCC ditemukan paling banyak pada stadium 2 (Soblin et al, 1997). Nilai p<0.038 menunjukkan ada hubungan bermakna antara staging tumor dengan kejadian metastasis pada RCC, hasil penelitian ini sama dengan penelitian sebelumnya yang mengatakan semakin tinggi staging tumor maka resiko terjadinya metastasis semakin besar dengan nilai p= 0.001 (Vina et al., 2016). **Simpulan:** Ada hubungan bermakna antara staging kanker ginjal dengan kejadian metastasis.

**Kata Kunci:** Renal cell carcinoma, faktor prediktor metastasis.

Correspondence: Moch. Abdul Kohar; c/o: Division of Urology/Department of Surgery, Faculty of Medicine/Gadjah Mada University, Sardjito General Hospital, Yogyakarta. Jl. Kesehatan No. 1, Yogyakarta. Phone: +62 274 587333; Fax: +62 274 543980. Email: abdulkohar2001@yahoo.com.

## INTRODUCTION

The incidence of Renal Cell Carcinoma (RCC) had showed an increase 2% annually over the past two decades. Renal Cell Carcinoma accounts

for 2-3% of all cancer cases worldwide and the third most common malignant, malignancy after prostate and bladder.<sup>1</sup>

It is the third leading cause of death in both the urogenital and 12<sup>th</sup> malignancies of cancer deaths

in the United States. According to Globocan data in 2008, the incidence of renal cancer in Indonesia is 2.4 over 100.000.<sup>2</sup> The number of RCC patients at Cipto Mangunkusumo Hospital (RSCM) in 1995-2009 amounted to 99 cases (33% of all cases of renal cancer). This number shows an increasing trend when data is seen every 5 years. In 1995-1999 there were 17 cases, in 2000-2004 as many as 30 cases, and in 2005-2009 as many as 52 cases.<sup>2</sup>

The prognostic factor is very important for the assessment of the RCC. Prognostic factors are divided into four categories, including anatomy, clinics, histology and molecular. For anatomy itself consists of tumor size, venous involvement to extension to other organs, adrenal gland, lymph node metastasis, distant metastasis. For clinical categories such as performance status, weight loss, anemia, hypercalcemia, elevated levels of lactate dehydrogenase (LDH), elevated levels of alkali phosphatase (ALP), increased erythrocyte sediments, thrombocytosis and increased C-reactive protein. For histology consisting of sub-type RCC, presence of necrotic tissue, perinefric invasion or renal fat, as well as invasion into renal pelvicalyses system. For the molecular consists of hypoxia-inducible factors, cell cycle regulators and other factors. Many studies have been done to determine the predictor factors of

metastasis and survival rate with mixed results, but no research has been done in Sardjito Hospital regarding metastasis as predictor for prognostic factor in RCC patients.

## OBJECTIVE

To analyze the association between various prognostic factors and the incidence of renal cell carcinoma metastasis.

## MATERIAL & METHODS

This is a descriptive retrospective study. In this research, the dependent variable is metastatic renal cell carcinoma, while the predictive factor for metastatic renal cell carcinoma as the independent variable. The study population was all patients with renal cell carcinoma at Sardjito Hospital period 2010-2015. The first step was descriptive analysis of research data; anatomical pathology, lymph node involvement, tumor staging based on TNM, anemia, LED, calcium, LDH, ALP. An analysis was carried out to assess the association between various prognostic factors and the incidence of renal cell carcinoma metastasis using SPSS 21.

## RESULTS

**Tabel 1.** Bivariate analyzes.

Variable	Metastase		P	C
	Yes	No		
Age				
<5 years old	3	13		
>5 years old	4	14	0.803	0.043
Weight loss				
Yes	3	7	0.381	
No	4	20	0.14	
Anatomical Pathology				
Clear	4	25		
Papillary	3	1	0.487	
Cromofob	0	1	0.443	
Tumor				
T2	0	15		
T3	1	5	0.038	
T4	6	7	0.46	
Anemia				
Normal	3	14		
Low	4	7	0.947	
Moderate	0	5	0.229	
Severe	0	1		
Rate sedimentation of blood				
High	7	24	0.356	
Normal	0	3	0.156	
ALP				
High	0	1	0.605	
Normal	7	26	0.088	
Calcium				
High	5	17	0.676	
Normal	2	10	0.071	
LDH				
High	1	9	0.324	
Normal	6	18	0.167	

**Table 2.** Characteristics of the research subjects.

Characteristics	Total	Percentage
Sex		
Male	20	58.8
Female	14	41.2
Weight loss		
Yes	10	29.4
No	24	70.6
Age		
<51 years old	16	47.1
>51 years old	18	52.9
Histological subtype		
Clear cell	29	85.3
Papillary	4	11.8
Chromophobe	1	2.9
TNM staging		
T2	15	44.1
T3	6	17.6
T4	13	38.2
Lymph node		
N0	27	79.4
N1	6	17.6
N2	1	2.9
Metastase		
Yes	6	17.6
No	28	82.4
Anemia		
Yes	17	50
No	17	50
Anemia		
Normal	17	50
Low	11	32.35
Moderate	5	14.71
Severe	1	2.94
Sedimentation rate of blood		
Yes	31	91.2
No	3	8.8
Calcium		
Yes	22	64.7
No	12	35.3
Lactate dehydrogenase (LDH)		
High	10	29.4
Normal	24	70.6
Alkali fustase(ALP)		
Yes	1	2.9
No	33	97.1

## DISCUSSION

In this study, the number of male with renal cell carcinoma as many as 20 cases and women 14 cases, our study found the same with previous research which states the ratio of incidence of men and women 3 : 2 and the average case in old age between six and seven decade.<sup>3</sup> From this study we obtained p value = 0.068 or not significant, so it can be concluded that there is no significant difference between incidence of men and women who suffer

from renal cell carcinoma. While for predictive factor category of age divided by 2 that is <51 years old and >51 years old, there is no significant relation with p value = 0.083. The results of this study are similar with previous studies which say there is no significant association between age with the incidence of metastasis in RCC with p value = 0.623.<sup>4</sup>

Most of RCCs have histologic subtype of clear cell carcinoma.<sup>5</sup> This study have the same result with our study. Our study found that, there were 29

(69.7%) cases with histologic clear cell subtype, 4 cases (11.8%) with papillary subtype and 1 case (2.9%) with chromophobe subtype. Each subtype of RCC has different biological profile. Clear cell types have a worse prognosis than papillary and chromophobe.<sup>6</sup>

Papillary RCC is divided into different subtypes of type 1 and type 2 that have different clinical course. Type 1 is a low grade tumor with a chromophilic cytoplasm with a good prognosis. Meanwhile, type 2 is almost all high grade tumors with eosinophilic cytoplasm with a large tendency to develop and metastasis. The p value = >0.487 indicates that there is no significant difference from the comparison of clear cell subtypes, papillary subtypes, to the cromophob subtype with the occurrence of metastasis.

In this study, patients with RCC mostly found in stage 2 with 15 cases (44.1%), stage 3 with 6 cases (17.6%), and stage 4 with 13 cases (38.2%). These results are consistent with previous studies which suggest that RCC is found most frequently in stage 2.<sup>7</sup> The p value = <0.038 indicates that there is a significant correlation between tumor staging and metastatic occurrence in RCC, the result of this study is similar to the previous study which stated that the higher the staging of the tumor the greater the risk of metastasis with p value = 0.001.<sup>4</sup>

In this study, we found there are no spread of lymph nodes (N0) as many as 27 cases (79.4%), for N1 as many as 6 cases (17.6%), while for N2 as much as 10 cases (2.9%). Our findings support previous studies,<sup>8</sup> which suggested that RCC is more common with no lymph node dissemination. In contrast to the retrospective studies conducted at Mayo Clinic,<sup>9</sup> which suggests high risk RCC is associated with spreading of lymph nodes or retroperitoneal lymphadenopathy.

In terms of metastasis aspects of renal cancer, our study found that stage 2 as many as 15 cases (44.1%), stage 3 with 6 cases (55.9%) and stage 4 with 13 cases. This is the same result with previous studies, where the RCC is commonly found when it has spread to the veins but not to the adrenal gland.<sup>8</sup>

In this study, there are as many as 7 cases (20.6%) have metastasis and 27 cases (79.4%) did not experience metastasis. These data reinforces previous research in Japan,<sup>9</sup> and United States. Metastasis was found in 25% and 23.4% cases.

In this study, the symptoms of anemia were obtained in 17 cases (50%), while without anemia

were 17 cases (50%) with no significant association between anemia symptoms and metastatic events in RCC patients with p value = 0.947. In contrast with the results of other studies,<sup>4</sup> showed significant association between anemia and metastasis in RCC patients with p value = 0.013. RCC patients with anemia had a poor prognosis compare with patients with RCC without anemia.<sup>10</sup> Trias symptoms in renal cancer, there are 3 namely pain in the waist, hematuria and palpable period in abdomen approximately 6-10%. Symptoms of hematuria affect the incidence of anemia in RCC patients.

In this study, we found the rate of sedimentation of blood obtained increase as many as 31 cases (91.2%) while the normal values of 3 cases (8.8%) with p value = >0.05. This showed that there is no significant difference from the increase of sedimentation of blood ratio with normal. Increased ESR is a poor prognostic factor in patients with RCC.<sup>11</sup>

In this study, calcium level was increased in 22 cases (64.7%). This finding, different with other studies,<sup>12</sup> which found that 60% of cases with increased level of calcium. In this study, the p value = >0.05, indicate that there was no significant difference in the ratio of calcium levels increase with normal calcium level. In this study, we also found the levels of LDH increased in 10 cases (29.4%). The results are slightly different from the previous study in which there is an increase in LDH in 60% of cases.<sup>13</sup> Our study found p value = >0.05, this indicate that there is no significant difference between elevated LDH level compare to normal LDH level.

In this study, ALP level increase by 1 person (2.9%) with p value = >0.05. This result means that there is no significant difference between the increase level of ALP levels to normal ALP level. These results are not the same as in some previous studies where an increase in ALP level in RCC cases was 60%.<sup>10</sup>

## CONCLUSION

There was a significant association between stage renal cancer and metastatic incidence.

## REFERENCES

1. Novick AC, Burowski RM, Campbell SC. Renal tumors. In: Kavoussi LR, Novick AC, Partin AV, Peters CA (eds) Wein AJ. Campbell-Walls Urology.

Philadelphia: WB Saunders; 2007. p. 1565-638.

2. Globocan 2008. <http://globocan.iarc.fr/factsheets/population/factsheet.asp?uno=360>. Disitasi December 15; 2014.
3. Steven D, Lynch J, Balaji KC. Increasing incidence of all stages of kidney cancer in the last 2 decades in the United States: An analysis of the Surveillance, Epidemiology and End Results program data. *J Urol.* 2002; 167: 57-60.
4. Vina, Agus R, Chaidir A, Rainy U. Clinical factors predictive of metastases from renal cell carcinomas. *Asian Pac J Cancer.* 2016; 17(9): 4503-6.
5. Singam P, Ho C, Goh EH, Mohd A, Tamil AZ, Lee BC, et al. Clinical characteristics of renal cancer in Malaysia: A ten year review. *Asian Pacific J Cancer Prev.* 2010; 11: 503-6.
6. Yasunaga, Masaru Shin, Okuyama. Prognostic factor of renal cell carcinoma. Japan; 1998.
7. Soblin LH, Wittekind C. TNM classification of malignant tumors, 5<sup>th</sup> Ed. New York: John Wiley; 1997.
8. Wassim M. Bazzi, Daniel D. Sjoberg. Long-term survival rates after resection for locally advanced kidney cancer. *J Urol.* June 2015; 193(6): 1911-7.
9. Kohsuke U, Noriomi M. Recurrence of renal cell carcinoma more than 5 years after nephrectomy. *Int J Urol.* 2002; 9: 19-23.
10. Srigley JR, Hutter RV, Gelb AB. Current prognostic factors—renal cell carcinoma: Work Group No. 4. Union Internationale Contre le Cancer (UICC) and the American Joint Committee on Cancer (AJCC). *Cancer.* 1997; 80: 994-6.
11. Hannisdal E, Bostad L, Grottum KA, Langmark F. Erythrocyte sedimentation rate as a prognostic factor in renal cell carcinoma. *Eur J Surg Oncol.* 1999; 15: 333-6.
12. Motzer RJ, Mazumdar M, Bacik J, Berg W, Amsterdam A, Ferrara J. Survival and prognostic stratification of 670 patients with advanced renal cell carcinoma. *J Clin Oncol.* 1999; 17(8): 2530-40.
13. Armstrong AJ, George DJ, Halabi S. Serum lactate dehydrogenase predicts for overall survival benefit in patients with metastatic renal cell carcinoma treated with inhibition of mammalian target of rapamycin. *J Clin Oncol.* 2012; 30(27): 3402-7.