CHARACTERISTICS OF RENAL CANCER PATIENTS IN HAJI ADAM MALIK GENERAL HOSPITAL MEDAN IN THE YEAR 2011 -2015

[1]Riyan Adi Kurnia, [2]Dhirajaya Dharma Kadar, [2]Fauriski Febrian Prapiska.

[1]Department of Urology, Faculty of Medicine/Universitas Indonesia, Cipto Mangunkusumo General Hospital, Jakarta.
[2]Division of Urology/Department of Surgery, Faculty of Medicine/Sumatera Utara University, Haji Adam Malik General Hospital, Medan.

ABSTRACT

Objective: *The aim of this study is to identity the characteristics of kidney cancer patients at Haji Adam Malik Hospital between 2011 and 2015.* ***Material & methods:*** *This is a retrospective descriptive study of all kidney cancer patients treated at Haji Adam Malik Hospital between 2011 and 2015. Individual patient data was collected from medical record and compiled.* ***Results:*** *Between 2011 and 2015, there were 38 patients diagnosed with kidney cancer treated at Haji Adam Malik Hospital. The patients mean age is 48.26 ± 14.68 years, with a male to female ratio 1.7:1. Histological type found in the study was RCC (57.15%), urothelium based (19.05%), sarcoma variant (14.28%) and benign kidney tumor (9.52%). Clear cell RCC (58.3%) is the most common type of RCC. Based on the TNM classification, patients with kidney tumor of stage II, stage III and stage IV are 15.8%, 10.5% and 73.7% respectively. The treatment modalities for kidney cancer are nephrectomy (44.7%), nephroureterectomy (2.6%), biopsy (8.0%) and inoperable patients or treatment refusal (44.7%). The mortality rate of kidney cancer patients was 81.5%.* ***Conclusion:*** *Mean age of kidney cancer patients at Haji Adam Malik Hospital was lower than that reported in literature. Gender ratio was found similar as seen in literature. The ratio of histological type was differ, but we still found RCC as the most common type of kidney malignancies. Higher number of patients presented at advance stage at diagnosis and refusal to treatment may contribute to the high mortality rate in this study.*

Key words: *kidney cancer.*

ABSTRAK

Tujuan: *Tujuan dari penelitian ini adalah untuk membuat data karakteristik pasien dengan tumor ginjal yang berobat ke RSUP H. Adam Malik Medan sejak tahun 2011 hingga 2015.* ***Bahan & cara:*** *Jenis penelitian ini adalah studi deskriptif retrospektif. Sampel penelitian adalah seluruh pasien yang telah didiagnosis dengan tumor ginjal yang berobat ke RSUP Haji Adam Malik tahun 2011 hingga 2015. Data dikumpulkan dari rekam medis.* ***Hasil:*** *Jumlah sampel yang dianalisis pada penelitian ini adalah 38 pasien. Rerata umur pasien adalah 48.26 ± 14.68 tahun, dengan rasio antara pasien laki-laki dengan perempuan adalah 1.7 : 1. Jenis histopatologi yang ditemukan pada penelitian ini adalah RCC (57.15%), urothelium based (19.05%), variasi dari sarcoma (14.28%) dan tumor ginjal jinak (9.52%). Tipe RCC yang terbanyak dijumpai adalah tipe Clear Cell RCC (58.3%). Berdasarkan sistem klasifikasi TNM, penderita tumor ginjal stage II, stage III dan stage IV terdapat 15.8%, 10.5% dan 73.7% secara berurutan. Jenis tatalaksana yang telah dilakukan pada pasien kanker ginjal adalah nefrektomi (44.7%), nefroureterektomi (2.6%), laparotomi biopsi (8.0%) dan pasien inoperable atau menolak tindakan operasi (44.7%). Tingkat mortalitas pasien kanker ginjal adalah 81.5%.* ***Simpulan:*** *Rerata usia pasien tumor ginjal di RSUP Haji Adam Malik lebih rendah dibandingkan dengan yang dilaporkan dalam literatur. Rasio jenis kelamin ditemukan serupa seperti dalam literatur. Rasio jenis histopatologis ditemukan berbeda, akan tetapi kami masih mendapatkan RCC sebagai jenis yang paling umum dari keganasan pada ginjal. Tingginya angka pasien yang berobat dengan stadium lanjut dan penolakan terhadap pengobatan mungkin berkontribusi terhadap tingginya tingkat mortalitas dalam penelitian ini.*

Kata Kunci: *Tumor ginjal.*

Correspondence: Riyan Adi Kurnia, c/o: Department of Urology, Faculty of Medicine/Universitas Indonesia, Cipto Mangunkusumo General Hospital, Jakarta. Jl. Diponegoro No. 71, Jakarta Pusat, DKI Jakarta 10430, Indonesia. Phone: +62 21 3152892, Fax: +62 21 3145592. Mobile phone: 0811860070. Email: riak_40@yahoo.com.

INTRODUCTION

Renal cancer is the third most common urology malignancy and is included as the ten most common type of malignancy. In the last three decades, incidence was constantly increasing in the United States and Europe with 54.390 new cases and 13.010 death due to renal cancer in 2008 in the United States. According to Globocan 2012, incidence of renal cancer in Indonesia reached 1.5/ 100.000 citizens.[1,2] Incidence of Renal Cell Carcinoma (RCC) was around 85% out of all renal malignancy. Transitional cell cancer was around 12% and other type of malignancy was 2%.[3]

Increasing incidence of renal cancer as time passes was not proportional to the relatively constant mortality rate in the United States. This is due to increase in incidental findings of renal cancer cases in early stages through abdominal imaging, which in turn makes an effective treatment more possible.[4] This increase in incidence especially occurred between women and African-American. Renal cancer happened twice more often between men than women, with mean age 60 years old.[5]

Risk factors related to renal cancer are smoking, obesity, and hypertension.[6] The risk increased with the presence of first degree relative who had renal cancer. A number of other factors that were suggested to have relation with renal cancer were dietary habits and carcinogen exposure, even though results from literature could not be concluded yet.[7,8] Alcohol consumption showed protective effects for reasons unknown yet.[9,10]

According to WHO classification year 2004 and ISUP Vancouver classification, renal cancer can be differentiated based on histo-pathological features. RCC consists of three main types, clear cell, papillary, and chromophobe. Other than those three types, there were still other types than are considered as rarer types of renal cancer.[11] Clear cell type had poorer prognosis than the other two types. The 5-year survival rate of each type was 73.2%, 79.4% and 87.9% for localized RCC.[12] Chromophobe type has better prognosis with lower risk of progressivity, metastasis, and cancer-specific death.[13]

Incidence and mortality rate differed between countries with various risk factors affecting renal cancer. Thus, it is needed to find out the characteristics of renal cancer patients in Haji Adam Malik General Hospital Medan.

OBJECTIVE

The aim of this study is to identity the characteristics of kidney cancer patients at Haji Adam Malik Hospital between 2011 and 2015.

MATERIAL & METHODS

This is a cross sectional descriptive study. The study was conducted in Haji Adam Malik General Hospital Medan. Subjects are patients diagnosed with renal cancer in the year 2011-2015. Data collected was analyzed using SPSS ver 23 and presented as tables and narration.

RESULTS

From the year 2011 until 2015 there were 38 patients diagnosed with renal cancer. According to sex, 24 patients were male, while 14 patients were female. There were 36 patients complaining of abdominal mass, 28 patients reported flank pain, and hematuria was found on 16 patients. Weight loss was experienced by 14 patients. Smoking habits was found on 24 patients (table 1).

Table 1. Characteristics of patients with renal cancer.

Variable	Total (%)
Sex	
Male	24 (63.16)
Female	14 (36.84)
Smoking	24 (63.16)
Complaints	
Hematuria	16 (42.10)
Flank pain	28 (73.68)
Abdominal mass	36 (94.74)
Weight loss	14 (36.84)

Mean age of patients was 48.26 ± 14.68 years old, with the youngest being 22 years old and the oldest 77 years old. The age group with the most renal cancer patients was 41-50 years old (figure 1).

In Table 2, mean BMI of patient was 21.58 ± 2.73 kg/m^2. Median of systolic blood pressure was 130 mmHg and diastolic blood pressure was 80 mmHg.

Imaging modality used in determining renal cancer diagnosis in this study were abdominal CT scan. Out of abdominal CT scan result for primary tumor staging, there were found 9 patients with T2 (2 patients T2a and 7 patients T2b), 6 patients with T3 (4 patients T3a and 2 patients T3b), and 23 patients with T4. Regional lymph node involvement

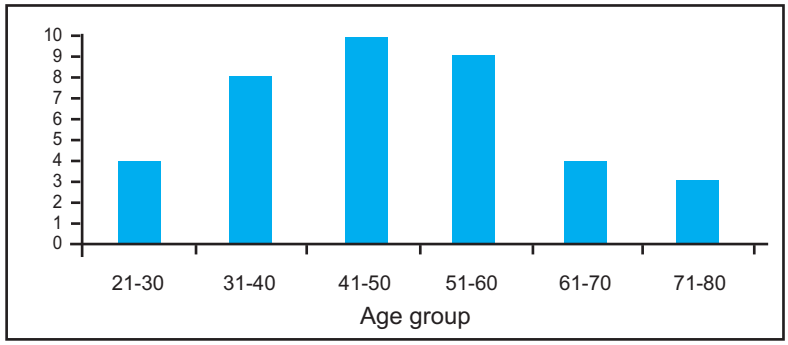

Figure 1. Age group of patients with renal cancer.

Table 2. Characteristics of age, BMI, and blood pressure on patients with renal cancer.

Variable	Mean	Min -Max
Age (years)	48.26 ± 14.68	22-77
BMI (kg/m^2)	21.58 ± 2.73	14.17 -26.99
Blood pressure (mmHg)	Median	
Systolic	130	110-190
Diastolic	80	70-110

was found in 14 patients and on 12 patients, remote metastasis was found. According to TNM classification, there were 6 renal cancer patients on stage II, 4 patients on stage III, and 28 patients on stage IV (table 3).

Table 3. Patients proportion based on staging.

Staging	Total
T: Primary tumor	
T1a	0
T1b	0
T2a	2
T2b	7
T3a	4
T3b	2
T3c	
T4	23
N: Regional lymph node	
N0	24
N1	14
M: Remote metastasis	
M0	26
M1	12
Stage Grouping	
Stage I	0
Stage II	6
Stage III	4
Stage IV	28

Out of 12 patients of renal cancer with remote metastasis, there were 8 patients with single metastasis and 4 patients with multiple metastasis. Metastasis locations included lungs on 7 patients, bone metastasis on 3 patients, liver metastasis on 6 patients, and brain metastasis on 1 patient (table 4).

Table 4. Metastasis proportion.

Metastasis	Total
Number of metastasis	
1	8
≥ 2	4
Metastasis location	
Lungs	7
Bone	3
Liver	6
Brain	1

In figure 2, out of 38 patients with renal cancer, 17 patients underwent nephrectomy, 1 patient had nephroureterectomy, 3 patients had laparotomy biopsy, and 17 patients had no surgery at all (either inoperable or refuse surgery).

From histopathological examination, renal mass findings were differentiated according whether it was malignant or benign. Benign renal cancers found in this study were angimyolipoma and lym-

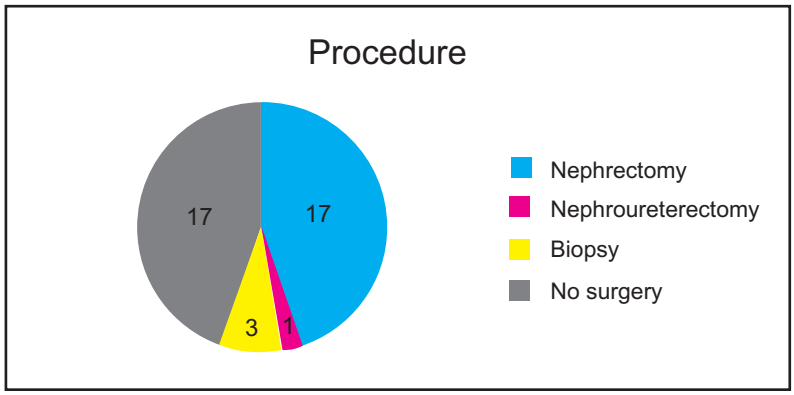

Figure 2. Type of procedure.

phoma, with each having 1 patient. Malignant renal cancer included Renal Cell Carcinoma, urothelium based, and variation of sarcoma. RCC types found were Clear Cell RCC on 7 patients, Papillary RCC on 3 patients, Chromophobe and Collecting Duct Carcinoma each on 1 patient. Urothelium based renal carcinoma found in this study were Squamous Cell Carcinoma on 3 patient and Transitional Cell Carcinoma on 1 patient. Meanwhile, the variations of sarcoma found were liposarcoma, Malignant Fibrous Histiocytoma, and nephroblastoma each on 1 patient (table 5).

Table 5. Histopathology.

Histopathology	Total
Malignant	
Renal Cell Carcinoma	
Clear Cell	7
Papillary	3
Chromophobe	1
Collecting Duct Carcinoma	1
Urothelium based	
Squamous Cell Carcinoma	3
Transitional Cell Carcinoma	1
Sarcoma	
Liposarcoma	1
Malignant Fibrous Histiocytoma	1
Nephroblastoma	1
Benign	
Angimiolipoma	1
Diifuse Large B Cell NHL	1

DISCUSSION

In this study, there were 24 male renal cancer patients, while there were 14 female patients. Renal cancer occurs 1.7 more often on males compared to females. This data is similar to the result of the study conducted by the International Agency for Research on Cancer, with male predominance twice more than female. Most patients with renal cancer was in age group 41-50 years old, more early than in the study conducted by Pantuck et al, in which the highest incidence was in the age group 60-70 years old.[5]

Most renal cancer patients were asymptomatic until they were in late stages. The classic triad was now rarely found on renal cancer patients. Out

Table 6. Incidence of complaints based on primary tumor stage.

Primary Tumor Stage	Hematuria	Flank Pain	Abdominal mass
T1a	0	0	0
T1b	0	0	0
T2a	0	2	1
T2b	4	4	6
T3a	2	2	4
T3b	1	2	2
T3c	0	0	0
T4	9	18	23

of the triad, the most common complaint was abdominal mass (94.74%) on almost every subjects in this study. Flank pain was usually caused by hemorrhage or clot obstruction, but may also occur as the tumor progress either locally or invasive. In table 6, it can be seen that most complaints were found in late primary tumor stage.

Risk factors for RCC are smoking, obesity, and hypertension, Proportion of renal cancer patients who smoked in this study was 63.16%. All forms of tobacco are known to be related to incidence of RCC and the risk increased with cumulative dose. Relative risk (RR) directly associated with smoking duration and duration of smoking cessation. Smokers or patients with smoking history had RR 1.38 compared to patients who had never smoked. The number of cigarettes, 1-9, 10-20 or ≥ 21 cigarettes per day had RR 1.6, 1.83, or 2.03 respectively. Meanwhile, the advantage of quitting smoking towards RR decrease was confirmed on people who had stopped smoking for at least >10 years, compared to those who stopped smoking for 1-10 years.[14]

There is a relationship between BMI and RCC risk with RR (per 5 kg/m^2 increase) 1.24 in males and 1.34 in females.[15] How obesity increased the risks of having RCC was still unclear. In this study, most patients with renal cancer had normal BMI and there was no obese renal cancer patient (table 7).

Table 7. BMI classification.

BMI (kg/m^2)	Classification	Total
<17	Severely underweight	1
17.0-18.5	Underweight	5
18.5-24.9	Normal	29
25.0-29.9	Overweight	3
30.0-34.9	Obesity level I	
35.0-39.9	Obesity level II	
>40	Obesity level III	

RCC risks with diastolic blood pressure ≥ 90 mmHg are more than two-fold higher compared to diastolic blood pressure <70 mmHg. Also for RCC, the risks are 60-70% higher in patients with systolic blood pressure ≥ 150 mmHg compared to systolic blood pressure of <120 mmHg.[16] Hypertension is defined as systolic blood pressure of ≥140 mmHg or diastolic blood pressure ≥ 90 mmHg, or having antihypertensive therapy. In this study, there were nine patients of renal cancer with hypertension (table 8).

Table 8. Blood pressure classification.

Blood pressure (mmHg)	Total
Diastolic	
<80	13
80-89	19
90-99	3
≥100	3
Systolic	
<120	10
120-139	18
140-159	5
≥160	4
Classification	
Normal	10
Pre-hypertension	19
Hypertension stage I	5
Hypertension stage II	4

Although ultrasound and abdominal CT scan have been highly developed, a lot of renal cancer cases went undetected until it was late, as most renal cancer cases were asymptomatic. Lesions found on the kidney of asymptomatic patient are mostly on early stages (stage I RCC, 62.1% incidental and 23% symptomatic), compared to patients who came with complaints related to RCC, which were commonly on late stages (stage IV RCC, 27.4% incidental and 54% symptomatic).[17] This is suitable with the result of this study, in which 23 patients were classified as stage T4 and all patients on that stage of disease complains of a symptom.

Lymph node involvement was determined from CT scan and intraoperative results. Regional lymph node involvement was found on 14 patients. Scoring for remote metastasis was determined from chief complaints, chest x-ray, and if needed, thorax CT scan or head CT scan. In this study, there were found 12 renal cancer patients with remote metastasis. Proportion of lymph node involvement and remote metastasis highly increase according to tumor size, especially when the tumor ≥1 cm.[18] This is consistent with the result of this study, in which proportion of regional lymph node involvement and remote metastasis highly increase according to the primary tumor stage.

Table 9. Proportion of regional lymph node involvement and metastasis based on primary tumor stage.

Primary Tumor Stage	N1	M1
T1a	0	0
T1b	0	0
T2a	0	0
T2b	3	2
T3a	1	0
T3b	1	1
T3c	0	0
T4	9	9

In a few diseases, young age was associated with a more aggressive disease. More aggressive disease may cause faster disease progression. On renal cancer, young age was associated with multiple metastasis.[19] In this study, the highest number of metastasis was found in age group 41-50 years old.

Curative therapy for renal cancer is radical nephrectomy. From patients who underwent nephrectomy, 6 patients were alive and 12 were deceased. Meanwhile, from patients who did not have nephrectomy, only 1 patient was alive while 19 other patients were deceased. Mortality rate of renal cancer patients was higher on patients who did not have nephrectomy compared to those who had. Advantage of nephrectomy on patient survival 5.2%, 6.5%, and 9.4% better on interval 1, 2, and 5 years post nephrectomy, consecutively.[20]

From histopathological examination, there were found RCC (57.15%), urothelium based (19.05%), variation of sarcoma (14.28%), and benign renal cancer (9.52%). RCC type most commonly found was Clear Cell RCC on 7 patients.

Table 11. Comparison of patients' survival between those who underwent nephrectomy and those who did not.

	Alive	Deceased
Nephrectomy	6	12
No nephrectomy	1	19

CONCLUSION

Mean age of patients with renal cancer in Haji Adam Malik General Hospital was lower than reported in literature. Ratio between sex was similar according to what was found in literature. Ratio between histopathologic types was different, although we still found that RCC was the most common type of renal malignancy. High number of patient seeking treatment in late stages and refusal towards treatment may contribute to the high mortality rate in this study.

REFERENCES

1. International Agency for Research on Cancer. Globocan 2012: Estimated cancer incidence, mortality and prevalence worldwide in 2012. Download from www.globocan.iarc.fr/Pages/fact_sheets_population.aspx
2. Colli J, Busby J, Amling C. Renal cell carcinoma rates compared with health status and behavior in the United States. J Urol. 2009; 73: 431-6.
3. Lipworth L, Tarone RE, McLaughlin JK. The epidemiology of renal cell carcinoma. J Urol. 2006; 176: 2353-8.
4. Chow W, Devesa S, Warren J. Rising incidence of renal cell cancer in the United States. JAMA. 1999; 281: 1628-31.
5. Pantuck AJ, Zisman A, Belldegrun AS. The changing natural history of renal cell carcinoma. J Urol. 2001; 166: 1611-23.
6. Ljunberg B, Campbell SC, Cho HY. The epidemiology of renal cell carcinoma. Eur Urol. 2011; 60: 615-21.
7. Weikert S, Boeing H, Pischon T. Fruits and vegetables and renal cell carcinoma: Findings from the European Prospective Investigation into Cancer and Nutrition (EPIC). Int J Cancer. 2006; 118: 3133-9.
8. Daniel C, Cross A, Graubard B. Large prospective investigation of meat intake, related mutagens, and risk of renal cell carcinoma. Am J Clin Nutr. 2012; 95: 155-62.

Table 10. Number of metastasis according to age group.

	21-30	31-40	41-50	51-60	61-70	71-80
Number of metastasis						
1	2	1	3	1	0	1
≥ 2	0	1	2	1	0	0

9. Bellocco R, Pasquali E, Rota M. Alcohol drinking and risk of renal cell carcinoma: Results of a meta-analysis. Annals of Oncol. 2012; 23: 2235-44.
10. Song D, Song S, Song Y. Alcohol intake and renal cell cancer risk: A meta-analysis. Brit J Cancer; 2012.
11. Srigley J, Delahunt B, Eble J. The International Society of Urology Pathology (ISUP) Vancouver Classification of Renal Neoplasia. Am J Surg Pathol. 2013; 37: 1469-89.
12. Steffens S, Janssen M, Roos F. Incidence and long-term prognosis of papillary compared to clear renal cell carcinoma – A multicentre study. Eur J Cancer. 2012; 48: 2347-52.
13. Volpe A, Novara G, Antonelli A. Chromophobe renal cell carcinoma (RCC): Oncological outcomes and prognostic factors in a large multicentre series. BJUI. 2011; 110(1): 76-83.
14. Hunt JD, van der Hel OL, McMillan GP. Renal cell carcinoma in relation to cigarette smoking: Meta-analysis of 24 studies. Int J Cancer. 2005; 114: 101-8.
15. Renehan AG, Tyson M, Egger M. Body-mass index and incidence of cancer: A systematic review and meta-analysis of prospective observational studies. Lancet. 2008; 371: 569-78.
16. Chow WH, Gridley G, Fraumeni JF. Obesity, hypertension, and the risk of kidney cancer in men. N Engl J Med. 2000; 343: 1305-11.
17. Tsui KH, Shvarts O, Smith RB. Renal cell carcinoma: A prognostic significance of incidentally detected tumors. J Urol. 2000; 163(2): 426-30.
18. Guðmundsson E, Hellborg H, Lundstam S. Metastatic potential in renal cell carcinomas ≤ 7 cm: Swedish Kidney Cancer Quality Register Data. Eur Urol. 2011; 60: 975-82.
19. Bianchi M, Sun M, Jeldres C. Distribution of metastatic sites in renal cell carcinoma: A population-based analysis. Annals of Oncol; 2011.
20. Zini L, Perrotte P, Jeldres C. A population-based comparison of survival after nephrectomy vs nonsurgical management for small renal masses. BJUI. 2009; 103: 899-904.