

Characteristics of renal cell carcinoma in Saudi patients below the age of 50 years

Saud Abdullah Alawad¹, Mohammed Hasen Alghamdi¹, Mohammed Ghazi Alharbi¹, Abdulmalik Addar^{1,2,3}, Abdullah M. Al Khayal^{1,2,3}, Ahmed Alasker^{1,2,3}

¹College of Medicine, King Saud Bin Abdulaziz University for Health Sciences, ²King Abdullah International Medical Research Center, ³Department of Surgery, Division of Urology, Ministry of the National Guard - Health Affairs, Riyadh, Saudi Arabia

Abstract

Background: The incidence of renal cell carcinoma (RCC) in young adults has started to increase in recent years.

Objectives: The objective of the study was to describe and compare the mode of presentation, incidence, risk factors, histopathological features, nephrectomy modalities used, and outcome in patients diagnosed with RCC below the age of 50.

Materials and Methods: A total of 139 confirmed RCC patients diagnosed below the age of 50 years who underwent nephrectomy from January 1990 to April 2019 were included in this retrospective review. We compared the characteristics of two age groups (≤ 40 years and 41–50 years) and evaluated incidentally discovered versus symptomatic tumors in patients below 50 years.

Results: Loin pain contributed to most symptomatic presentations in the older group (55%) ($P = 0.014$). Hypertension and diabetes were present in 24% of patients from 41 to 50 years of age versus 3.8% for hypertension and 5.7% for diabetes in the young group. ($P = 0.001$ and $P = 0.004$, respectively). Chromophobe was the second most common pathology (26.5%). Tumor size tended to be larger in the older group ($P = 0.006$). Fuhrman's grade was significantly lower in incidentally diagnosed patients (88.2%) ($P = 0.006$). The T stage was significantly lower in the incidental group ($P = 0.005$), but the mortality rate was higher in symptomatic patients (9.6%) ($P = 0.013$).

Conclusion: RCC increases after the age of 40–50 years in the presence of other risk factors. Chromophobe represented almost a quarter percentage of the pathology, while partial nephrectomy yielded a better outcome.

Keywords: Incidence, partial nephrectomy, radical nephrectomy, renal cell carcinoma, young adults

Address for correspondence: Dr. Saud Abdullah Alawad, College of Medicine, King Saud Bin Abdulaziz University for Health Sciences, Riyadh, Saudi Arabia. E-mail: AlawadSAH@gmail.com

Received: 14.01.2021, **Accepted:** 23.05.2021, **Published:** 28.12.2021.

INTRODUCTION

In Saudi Arabia, kidney tumor incidence and its associated mortality account for 3.4% and 2.4% of the population, respectively, favoring male gender and elderly

individuals.^[1] Approximately 85% of kidney tumors are renal cell carcinoma (RCC).^[2] RCC can be histologically subdivided into the clear cell, papillary, and chromophobe, representing more than 90% of all RCC cases.

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

For reprints contact: WKHLRPMedknow_reprints@wolterskluwer.com

How to cite this article: Alawad SA, Alghamdi MH, Alharbi MG, Addar A, Al Khayal AM, Alasker A. Characteristics of renal cell carcinoma in Saudi patients below the age of 50 years. *Urol Ann* 2022;14:15-20.

Access this article online	
Quick Response Code:	Website: www.urologyannals.com
	DOI: 10.4103/ua.ua_14_21

The average age for RCC incidence is 61 years, with only a minor percentage (5%) in the younger age group.^[3] Variations of causes, risk factors, clinical and pathological presentations, recurrence, and prognosis among the young group require clarification.^[4]

This study aims to determine the incidence, characteristics, and prognosis of RCC among patients below 50 years in Saudi Arabia.

MATERIALS AND METHODS

This study was conducted in a tertiary hospital in Riyadh, Saudi Arabia. We retrospectively reviewed the data records of all RCC patients between the ages of 20 and 50 years who were pathologically diagnosed with RCC and underwent open, laparoscopic, or robotic-assisted partial or radical nephrectomy surgery from January 1990 to April 2019. We included adult patients with primary RCC between the ages of 18 and 50 years. Any patient who did not have a confirmed pathological report of RCC was excluded.

Data, including age, sex, body mass index, nephrectomy type and date, mode of presentation, past medical history, histological, and pathological characteristics, were collected. Histopathology report based on biopsy obtained after performing the nephrectomy by any surgical mean included Fuhrman grade; primary tumor, nodal involvement, and metastatic involvement (TNM) stage of the lesion; and tumor size, which was recorded as the longest dimension of the lesion measured on pathologic examination. All RCCs were staged according to the American Joint Commission on Cancer 1997 TNM staging system and graded using the Fuhrman grading system.^[5,6] The patient follow-up for recurrence, site of recurrence, and death rate were obtained from medical charts.

Descriptive data are presented as mean (standard deviation) or median (interquartile range) for continuous variables and *n* (%) for categorical variables. *P* < 0.05 was considered statistically significant. Statistical analysis was performed using the IBM Corp., Released 2016, IBM SPSS Statistics for Windows, Version 24.0. Armonk, NY: IBM Corp.

RESULTS

Table 1 shows the demographic data of the patients along with a comparison of the younger age group (≤40 years) and older age group (41–50). A total of 139 patients were included in the study, with a male-to-female ratio of almost 2:1. The mean age at diagnosis was 42 ± 7 and ranged from 20 to 50 years. The age group ≤40 was 53 patients (38.1%),

and age group from 41 to 50 was 86 patients (61.9%) of the included population. The majority of patients were male (59.7%).

The RCC cases were divided into six groups, each representing 5 years, from 1990 to 2019. The distribution of RCC cases was as follows: 1990–1994, 7 cases (5%); 1995–1999, 11 cases (7.9%); 2000–2004, 14 cases (10.1%); 2005–2009, 19 cases (13.7%); 2010–2014, 45 cases (32.4%); and 2015–2019, 43 cases (30.9%). RCC incidence was found to be significantly increased over the years, particularly in the older group (41–50) (*P* < 0.031).

Nearly 50% of the patients were obese, and 35.4% were overweight. Regarding risk factors, 24 (17.3%) of the total patient population had diabetes, 23 (16.5%) had hypertension, and 12 were smokers (15%). In an age comparison, diabetes was significantly associated with the older age group between 40 and 50 years (24.4%), while it was present in only 5.7% of the younger patients ≤40 years (*P* < 0.004). Furthermore, the incidence of hypertension was significantly increased in the older group, representing 24.4%, while only observed in 3.8% of the younger patients (*P* < 0.006).

About 93 (71%) underwent radical nephrectomy, and 75 (55.1%) were symptomatic, with an increase in symptomatic presentation in the older group. Symptomatic patients presented with loin pain (44.1%), followed by hematuria (18.6%). Comparing the symptoms at presentation between the two groups, loin pain was significantly associated with patients over the age of 41–50, representing 55% (*P* < 0.014). However, hematuria was more prevalent in younger patients (31.6%), while in the older age group, it was only (12.5%).

The histopathology report revealed that 25% of patients had tumors invading the renal sinus, and 12% had lymphovascular invasion, while only 1.7% of the patients had tumors reaching the collecting system. Furthermore, RCC histology subtypes were mostly clear cell carcinoma (66.2%), followed by chromophobe (26.5%), papillary carcinoma (6.6%), and unclassified RCC was 0.7%. Patients were mostly diagnosed as pT1 stage (56.4%), followed by T3 (23.3%). Only 2.4% of patients had metastasis to the lymph node and nodal metastasis (42.7%). Metastasis was not identified in the vast majority of patients (67.5%), while M0 accounted for 28.9%, and M1 accounted for 3.6% of all patients. The Fuhrman grade was low in 75.7% of patients, and 10.5% had a positive surgical margin.

Table 1: Demographic data and comparison between younger group (≤40) and older group (41-50)

Variables	n (%)	Age at diagnosis		P
		≤40, n (%)	41-50, n (%)	
Gender				
Female	56 (40.3)	24 (45.3)	32 (37.2)	0.346
Male	83 (59.7)	29 (54.7)	54 (62.8)	
RCC cases in 5 years interval				
1990-1994	7 (5.0)	2 (3.8)	5 (5.8)	0.031*
1995-1999	11 (7.9)	9 (17.0)	2 (2.3)	
2000-2004	14 (10.1)	7 (13.2)	7 (8.1)	
2005-2009	19 (13.7)	5 (9.4)	14 (16.3)	
2010-2014	45 (32.4)	17 (32.1)	28 (32.6)	
2015-2019	43 (30.9)	13 (24.5)	30 (34.9)	
Smoking				
No	68 (85.0)	27 (79.4)	41 (89.1)	0.229
Yes	12 (15.0)	7 (20.6)	5 (10.9)	
BMI				
Underweight	0	0	0	0.179
Normal	12 (14.6)	7 (24.1)	5 (9.4)	
Overweight	29 (35.4)	10 (34.5)	19 (35.8)	
Obese	41 (50.0)	12 (41.4)	29 (54.7)	
Nephrectomy type				
Radical	93 (71.0)	35 (71.4)	58 (70.7)	0.932
Partial	38 (29.0)	14 (28.6)	24 (29.3)	
Procedure type				
Open	69 (51.5)	28 (54.9)	41 (49.4)	0.688
Laparoscopy	56 (41.8)	19 (37.3)	37 (44.6)	
Robotic	9 (6.7)	4 (7.8)	5 (6.0)	
Clinical presentation				
Symptomatic	75 (55.1)	23 (45.1)	52 (61.2)	0.068
Incidental	61 (44.9)	28 (54.9)	33 (38.8)	
Hematuria				
No	48 (81.4)	13 (68.4)	35 (87.5)	0.079
Yes	11 (18.6)	6 (31.6)	5 (12.5)	
Loin pain				
No	33 (55.9)	15 (78.9)	18 (45.0)	0.014*
Yes	26 (44.1)	4 (21.1)	22 (55.0)	
Hypertension				
No	116 (83.5)	51 (96.2)	65 (75.6)	0.001*
Yes	23 (16.5)	2 (3.8)	21 (24.4)	
Diabetes				
No	115 (82.7)	50 (94.3)	65 (75.6)	0.004*
Yes	24 (17.3)	3 (5.7)	21 (24.4)	
Histology				
Lymphovascular invasion	7 (11.9)	2 (10.5)	5 (12.5)	0.827
Renal sinus invasion	15 (25.4)	3 (15.8)	12 (30.0)	
Collecting system	1 (1.7)	0	1 (2.5)	
Nature of lesion				
Clear cell	90 (66.2)	36 (67.9)	54 (65.1)	0.822
Papillary	9 (6.6)	4 (7.5)	5 (6.0)	
Chromophobe	36 (26.5)	13 (24.5)	23 (27.7)	
Unclassified RCC	1 (0.7)	0 (0.0)	1 (1.2)	
Surgical margin				
Negative	51 (89.5)	19 (100.0)	32 (84.2)	0.067
Positive	6 (10.5)	0	6 (15.8)	
Furhman grade				
Low	81 (75.7)	33 (84.6)	48 (70.6)	0.103
High	26 (24.3)	6 (15.4)	20 (29.4)	
Tumor size (cm)				
≤4	28 (33.3)	14 (48.3)	14 (25.5)	0.006*
>4 and≤7	27 (32.1)	11 (37.9)	16 (29.1)	
>7 and<10	12 (14.3)	4 (13.8)	8 (14.5)	
≥10	17 (20.2)	0 (0.0)	17 (30.9)	
Mortality				
No	130 (94.9)	50 (96.2)	80 (94.1)	0.599
Yes	7 (5.1)	2 (3.8)	5 (5.9)	

Contd...

Table 1: Contd...

Variables	n (%)	Age at diagnosis		P
		≤40, n (%)	41-50, n (%)	
Recurrence				
No	122 (90.4)	46 (90.2)	76 (90.5)	0.957
Yes	13 (9.6)	5 (9.8)	8 (9.5)	
Site of recurrence				
None	56 (84.8)	18 (78.3)	38 (88.4)	0.199
Local	1 (1.5)	1 (4.3)	0	
Distal	7 (10.6)	4 (17.4)	3 (7.0)	
Both	2 (3.0)	0 (0.0)	2 (4.7)	
T				
T1	75 (56.4)	32 (64.0)	43 (51.8)	0.399
T2	20 (15.0)	8 (16.0)	12 (14.5)	
T3	31 (23.3)	8 (16.0)	23 (27.7)	
T4	7 (5.3)	2 (4.0)	5 (6.0)	
N				
N0	35 (42.7)	12 (42.9)	23 (42.6)	0.888
N1	2 (2.4)	1 (3.6)	1 (1.9)	
N2	0	0	0	
N3	0	0	0	
Nx	45 (54.9)	15 (53.6)	30 (55.6)	
M				
M0	24 (28.9)	11 (37.9)	13 (24.1)	0.217
M1	3 (3.6)	0 (0.0)	3 (5.6)	
Mx	56 (67.5)	18 (62.1)	38 (70.4)	

*significant at 5% level, RCC: Renal cell carcinoma, BMI: Body mass index

Regarding tumor size, tumors equal to or <4 cm were present in 33.3% of the cases, followed by >4 to ≤7 cm (32.1%), ≥10cm (20.2%), and >7 to <10 cm (14.3%). There was no significant difference in tumor diameter between the young group and the older group, although the younger age group tended to present with smaller tumor size. Tumors sized ≤4 cm, >4 to ≤7 cm, >7 to <10 cm, and ≥10 cm were present in 48.3%, 37.9%, 13.8%, and 0% of the younger cases, respectively. However, the majority of the older age group tended to have tumors ≥10 cm at the time of diagnosis (30.9%), followed by tumors sized 4 to ≤7 (29.1%), ≤4 (25.5%), and >7 to <10 (14.5%) ($P < 0.006$).

Other variables were not statically significant in the comparison between the two age groups such as nephrectomy type, nature of the lesion, surgical margin, Furman grade, invasion of lymphovascular tissue, renal sinuses, the collecting system, recurrence, mortality, and TNM stage.

In Table 2, we compared incidental versus symptomatic presentation in patients diagnosed with RCC below the age of 50. Most patients (79.4%) presented with symptoms that were managed by radical nephrectomy ($P < 0.016$). In comparison to symptomatic patients, incidentally discovered tumors were found to have a low Furhman grade at the time of diagnosis ($P = 0.006^*$). In addition, around 70% of incidentally discovered tumors presented with lower T stage ($P < 0.005$). The average mean diameter of incidentally discovered tumors was 5.62 (± 3 cm),

while the average mean size of symptomatic tumors was 7.50 (± 4 cm) ($P = 0.0178$). Mortality in incidentally discovered tumors after surgical treatment was (0%), whereas, in symptomatic tumors, it was around 10% ($P < 0.013$). There were no significant differences in the nature of the lesion between symptomatic and incidental findings.

DISCUSSION

This study is the first local study to define the presentation and histopathological features and outcomes of surgical modalities in patients diagnosed with RCC below the age of 50 years.

The incidence of RCC is trending up both globally and locally in recent years, especially in younger age groups.^[1,7-9] One study linked the rise of RCC cases to an increase in the incidence of low risk cancers such as pT1a tumors that can be explained on the basis of ascertainment bias due to the overdiagnosis of small renal masses.^[10] Other risk factors may be specific genetic and environmental factors along with obesity, smoking, and occupational exposure.^[11] In addition, the use of advanced radiological modalities in detecting renal masses has contributed to an increased level of incidental findings of RCC, which increases the overall incidence of RCC, especially for tumors measuring 4 cm or less.^[12,13] In our study, we found that there was a significant increase in RCC in young patients below the age of 50 years over the past 30 years, especially between the years 2010 and 2019.

Table 2: Incidental versus symptomatic presentation comparison regarding procedure type, histology, and tumor characteristics in patients diagnosed with renal cell carcinoma below the age of 50

Variables	Clinical presentation		P
	Symptomatic, n (%)	Incidental, n (%)	
Nephrectomy type			
Radical	54 (79.4)	36 (60.0)	0.016*
Partial	14 (20.6)	24 (40.0)	
Nature of lesion			
Clear cell	47 (65.3)	40 (65.6)	0.620
Papillary	6 (8.3)	3 (4.9)	
Chromophobe	19 (26.4)	17 (27.9)	
Unclassified RCC	0	1 (1.6)	
Fuhrman grade			
Low	36 (65.5)	45 (88.2)	0.006*
High	19 (34.5)	6 (11.8)	
Tumor size (cm) (mean±SD)	7.50±4	5.62±3	0.0178*
Tumor size (cm)			
≤4	12 (27.3)	16 (40.0)	0.120
>4 and≤7	12 (27.3)	15 (37.5)	
>7 and<10	7 (15.9)	5 (12.5)	
≥10	13 (29.5)	4 (10.0)	
Mortality			
No	66 (90.4)	61 (100.0)	0.013*
Yes	7 (9.6)	0	
T (stage)			
T1	32 (44.4)	43 (71.7)	0.005*
T2	13 (18.1)	6 (10.0)	
T3	20 (27.8)	11 (18.3)	
T4	7 (9.7)	0	

*significant at 5% level, RCC: Renal cell carcinoma, SD: Standard deviation

There are conflicting reports regarding the presentation of RCC in the literature. Several studies have reported that younger patients are more likely to present symptomatically.^[11,14] In contrast, others studies noticed more incidental presentation in the younger group.^[3,4] In our study, approximately 55% of patients in the older group presented with symptoms. There was no statistically significant variation in the presentation in comparison with the younger group. In addition, we found that the older group had a high tendency to present with loin pain, which was reported in another study.^[15] While several studies reported that loin pain was the most common presentation in the young group,^[15-17] we found hematuria accounted for a higher percentage. This finding is in line with a previous study as well.^[3]

Our study showed an increase in diabetes and hypertension in patients in the 41–50-year age group. A recent meta-analysis and closer scrutiny of the cancer type reveal a close association of RCC with hypertension, which increased to around 20%–30%. In another study, about 500,000 Korean men participated, and it proved hypertension to be a strong and independent risk factor for kidney cancer mortality.^[18] A meta-analysis of 18 studies showed a positive association between diabetes

and kidney cancer.^[19] A recent study suggested a significant increase in the risk of RCC among diabetic women. In fact, RCC in patients with Type 2 diabetes shows more DNA alterations when compared with RCC inpatients without Type 2 diabetes.^[20]

Young patients diagnosed with RCC tended to present with low Fuhrman grade tumors. In a study conducted in patients younger than 45 years of age with RCC, tumors with low Fuhrman grade represented almost 75% of the total cases.^[16] Similarly, in our study, most RCC patients below the age of 50 had a low Fuhrman grade (76%). Moreover, in patients below the age of 40 years, approximately 85% of cases had a low Fuhrman grade. In addition, a study reported that younger patients had significantly lower Fuhrman grades than those aged 40–60 years.^[21]

The clear cell subtype was dominant in our study, and no significant difference was found when comparing the two age groups (67.9% vs. 65.1%). This is in line with other studies but with different percentages.^[3,4,22] The second most common RCC subtype in our study was the chromophobe subtype, accounting for 26%. This was also observed in other studies.^[14,21,23] This is an advantage with regard to prognosis, given that chromophobe has a less aggressive nature and a favorable prognosis.^[24] However, other studies reported that papillary is the second most common histology subtype.^[25,26] Racial variation in the histology subtypes of renal RCC has been addressed in several studies, probably because of differences in multiple RCC prognostic factors.^[4,9,10]

Based on our results, we observed that the mode of presentation had an impact on the surgical modality that was used to manage the tumor. We found that incidentally diagnosed patients were managed more with partial nephrectomy compared to the group who presented with symptoms. This may be explained by the incidental group in our study presented with low Fuhrman grade, small tumor diameter, and low T stage. Furthermore, the mortality rate was significantly lower in the incidental group than in the symptomatic group [Table 2]. This finding was supported by a meta-analysis conducted in 2016. In this meta-analysis, a total of 21 reviews were included, and a comparison between partial and radical nephrectomy in T1b and T2 was performed. It was found that partial nephrectomy had a better prognosis in terms of renal function and a lower probability of chronic kidney disease. Moreover, they had a lower recurrence rate and lower mortality than their peers who underwent radical nephrectomy.^[27]

CONCLUSION

We concluded that RCC surges simultaneously with

hypertension and diabetes after the age of 40 years. Around 27% of young patients with RCC tend to present with chromophobe subtypes, which are less aggressive and have a favorable prognosis. However, clear cell carcinoma still accounts for most RCC cases. Surgical management with partial nephrectomy when feasible yields a lower recurrence rate and increase overall survival.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

- Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin* 2018;68:394-424.
- Gupta K, Miller JD, Li JZ, Russell MW, Charbonneau C. Epidemiologic and socioeconomic burden of metastatic renal cell carcinoma (mRCC): A literature review. *Cancer Treat Rev* 2008;34:193-205.
- Goetzl MA, Desai M, Mansukhani M, Goluboff ET, Katz AE, Sawczuk IS, *et al.* Natural history and clinical outcome of sporadic renal cortical tumors diagnosed in the young adult. *Urology* 2004;63:41-5.
- Kang HW, Seo SP, Kim WT, Yun SJ, Lee SC, Kim WJ, *et al.* Impact of young age at diagnosis on survival in patients with surgically treated renal cell carcinoma: A multicenter study. *J Korean Med Sci* 2016;31:1976-82.
- Fuhrman SA, Lasky LC, Limas C. Prognostic significance of morphologic parameters in renal cell carcinoma. *Am J Surg Pathol* 1982;6:655-63.
- Guinan P, Sobin LH, Algaba F, Badellino F, Kameyama S, MacLennan G, *et al.* TNM staging of renal cell carcinoma: Workgroup No. 3. Union International Contre le Cancer (UICC) and the American Joint Committee on Cancer (AJCC). *Cancer* 1997;80:992-3.
- Alkhateeb SS, Alothman AS, Addar AM, Alqahtani RA, Mansi TM, Masuadi EM. Kidney cancer in Saudi Arabia. A 25-year analysis of epidemiology and risk factors in a tertiary center. *Saudi Med J* 2018;39:459-63.
- Mahasin SZ, Aloudah N, Al-Surimi K, Alkhateeb SS. Epidemiology profile of renal cell carcinoma: A 10-year patients' experience at King Abdulaziz Medical City, National Guard Health Affairs, Saudi Arabia. *Urol Ann* 2018;10:59-64.
- Znaor A, Lortet-Tieulent J, Laversanne M, Jemal A, Bray F. International variations and trends in renal cell carcinoma incidence and mortality. *Eur Urol* 2015;67:519-30.
- Palumbo C, Pecoraro A, Rosiello G, Luzzago S, Deuker M, Stolzenbach F, *et al.* Renal cell carcinoma incidence rates and trends in young adults aged 20-39 years. *Cancer Epidemiol* 2020;67:101762.
- Abou El Fettouh HI, Cherullo EE, El-Jack M, Al Maslamani Y, Novick AC. Sporadic renal cell carcinoma in young adults: Presentation, treatment, and outcome. *Urology* 2002;60:806-10.
- Patard JJ. Incidental renal tumours. *Curr Opin Urol* 2009;19:454-8.
- Smith-Bindman R, Miglioretti DL, Johnson E, Lee C, Feigelson HS, Flynn M, *et al.* Use of diagnostic imaging studies and associated radiation exposure for patients enrolled in large integrated health care systems, 1996-2010. *JAMA* 2012;307:2400-9.
- Gillett MD, Cheville JC, Karnes RJ, Lohse CM, Kwon ED, Leibovich BC, *et al.* Comparison of presentation and outcome for patients 18 to 40 and 60 to 70 years old with solid renal masses. *J Urol* 2005;173:1893-6.
- Denzinger S, Otto W, Burger M, Hammerschmied C, Junker K, Hartmann A, *et al.* Sporadic renal cell carcinoma in young and elderly patients: Are there different clinicopathological features and disease specific survival rates? *World J Surg Oncol* 2007;5:16.
- Eggenger SE, Rubenstein JN, Smith ND, Nadler RB, Kontak J, Flanigan RC, *et al.* Renal tumors in young adults. *J Urol* 2004;171:106-10.
- Zugor V, Fridel S, Lausen B, Schott GE, Kühn R, Labanaris AP. Renal cell carcinoma under 35 years of age: Comparison of survival rates for symptomatic and asymptomatic patients. *Int Urol Nephrol* 2008;40:289-93.
- Messerli FH. Risk factors for renal cell carcinoma: Hypertension or diuretics? *Kidney Int* 2005;67:774-5.
- Chen L, Li H, Gu L, Ma X, Li X, Gao Y, *et al.* The Impact of Diabetes Mellitus on Renal Cell Carcinoma Prognosis: A Meta-Analysis of Cohort Studies. *Medicine (Baltimore)* 2015;94:e1055.
- Graff RE, Sanchez A, Tobias DK, Rodríguez D, Barrisford GW, Blute ML, *et al.* Type 2 diabetes in relation to the risk of renal cell carcinoma among men and women in two large prospective cohort studies. *Diabetes Care* 2018;41:1432-7.
- Jeong IG, Yoo CH, Song K, Park J, Cho YM, Song C, *et al.* Age at diagnosis is an independent predictor of small renal cell carcinoma recurrence-free survival. *J Urol* 2009;182:445-50.
- Thompson RH, Ordonez MA, Iasonos A, Secin FP, Guillonneau B, Russo P, *et al.* Renal cell carcinoma in young and old patients—is there a difference? *J Urol* 2008;180:1262-6.
- Lopez JI, Moreno V, Garcia H, Anton I, Robles A, Onate JM, *et al.* Renal cell carcinoma in young adults: A study of 130 cases and a review of previous series. *Urol Int* 2010;84:292-300.
- Peyromaure M, Misrai V, Thiounn N, Vieillefond A, Zerbib M, Flam TA, *et al.* Chromophobe renal cell carcinoma: Analysis of 61 cases. *Cancer* 2004;100:1406-10.
- Taccoen X, Valeri A, Descotes JL, Morin V, Stindel E, Doucet L, *et al.* Renal cell carcinoma in adults 40 years old or less: Young age is an independent prognostic factor for cancer-specific survival. *Eur Urol* 2007;51:980-7.
- Verhoest G, Veillard D, Guillé F, De La Taille A, Salomon L, Abbou CC, *et al.* Relationship between age at diagnosis and clinicopathologic features of renal cell carcinoma. *Eur Urol* 2007;51:1298-304.
- Mir MC, Derweesh I, Porpiglia F, Zargar H, Mottrie A, Autorino R. Partial nephrectomy versus radical nephrectomy for clinical T1b and T2 renal tumors: A systematic review and meta-analysis of comparative studies. *Eur Urol* 2017;71:606-17.